Design and Synthesis of Potential ARTD8 inhibitors towards the treatment of Metastatic Prostate Cancer

Tauber, Amanda L; Schweiker, Stephanie S; Levonis, Stephan M

3rd Queensland Annual Chemistry Symposium
QACS 2018

Friday 23rd November 2018
8:30am – 5:30pm

Griffith University
Nathan Campus
Kessels Road, Nathan, Queensland, Australia

Programme

A copy of this programme and abstracts will also available online at
https://www.raci.org.au/events/event/qacs2018-qld-annual-chemistry-symposium

The organising committee:

Assoc Prof Sarah Cresswell (Co-Chair) ▪ Assoc Prof Mark Coster (Co-Chair)
Dr Romain Lepage (Treasurer) ▪ Dr Todd Houston ▪ Assoc Prof John McMurtrie
Dr Angela DiCapua ▪ Katarzyna Kepa ▪ Kristina Julia Jovic
▪ Cohan Huxley

We thank our generous sponsors

Griffith University

RACI Queensland Branch

.

.

.

Morning Programme

Registrations will commence from 8:00am	**Venue: Central Theatres Atrium**
Morning Plenary Session - Chair: Sarah Cresswell	**Venue: Central Theatres (N18_Th2)**
8:45	**Opening remarks:** Mark Coster
8:50	**Plenary lecture P1: Professor Debra Bernhardt** – University of Queensland – *Theoretical and computational molecular science: from non-equilibrium systems to materials for sustainable energy applications*
9:30	**Plenary lecture P2: Associate Professor Kathryn Fairfull-Smith** – Queensland University of Technology *Controlling Bacterial Biofilms with Nitroxides*
10:10	**Morning tea** **Venue: Mezzanine Level (N76)**

Morning Parallel Sessions	
	Medicinal Chemistry - Chair: Todd Houston **Venue: Central Theatres (N18_Th 2)**
10:30	A1 **Mohit Chhabra** (UQ) *Probing the interactions of amphiphilic heparan sulfate mimetics with heparanase*
10:45	A2 **Conan K Wang** (UQ) *You better shape up, 'cause I need a drug*
11:00	A3 **Jianying Han** (GU) *Exploring the potential of endophytes and fungi as sources of anti-mycobacterial compounds*
11:15	A4 **Tamim Mosaiab** (GU) *Glycolipid-based nanostructures for macrophage targeted antimicrobial drug delivery*
11:30	A5 **Iftekhar Ahmed** (UQ) *New flavonoids and saponins from Gynostemma pentaphyllum (Thunb.) Makino*
11:45	A6 **Waleed Hussein** (UQ) *Novel prodrugs against Mycobacterium tuberculosis ketol-acid reductoisomerase (KARI)*
12:00	A7 **Miaomiao Liu** (GU) *Anti-TB natural products identification using native mass spectroscopy*
12:15	*End of session*
	Analytical, Food and Chemistry Education – Chair: Sarah Cresswell **Venue: Campus Heart N76_1.04**
10:30	B1 **Saiqa Muneer** (QUT) *Rapid bio-sensing of antibody drugs in human plasm*
10:45	B2 **Hyo Jeong Minnie Kim** (BondU) *Investigation of salivary sialic acid as a biomarker in obesity: determination of both free and protein-bound 5-N-acetylneuraminic (Neu5Ac) and 5-N-glycolylneuraminic (Neu5Gc) sialic acids in human saliva*
11:00	B3 **Gabriele Netzel** (UQ) *Indospicine residues in meat and liver from Western Australia cattle – a survey and risk assessment*
11:15	B4 **Lukas Michalek** (QUT) *Exploring the limits of surface grafting*
11:30	B5 **Kai Mundsinger** (QUT) *Understanding the limits of grafting-To*
11:45	B6 **Sadia A Chowdhury** (UQ/QH) *Authentication of Australian honey (don't believe the headlines)*
12:00	B7 **Andrew Pearson** (GU) *Strategic engagement of foundation year health students with chemistry*
12:15	*End of session*

Morning Parallel Sessions cont.		
	Materials, Inorganic and Theoretical Chemistry – Chair: Ashley Tronoff	**Venue: Campus Heart N76_1.05**
10:30	C1 **Katrin B Kockler** (QUT) *Glow stick chemistry: making and breaking bonds with chemiluminescence*	
10:45	C2 **Jessica K Bilyj** (UQ) *Nickel bis(dithiocabazates): the rebel child of the N,S-chelating family*	
11:00	C3 **Marco Pandullo** (QUT) *Metallosupramolecular polyhedral for inclusion in multicomponent co-crystals*	
11:15	C4 **Kristina J Jovic** (QUT) *Correlating in-depth mechanistic understanding with mechanical properties of high-temperature resistant cyclic imide copolymers*	
11:30	C5 **Hong Duc Pham** (QUT) *Small molecular hole transporting materials for inverted perovskite solar cells*	
11:45	C6 **Yu Ling Zhong** (GU) *Scalable Production of graphene oxide via 3D-printed packed-bed electrochemical reactor with boron-doped diamond anode*	
12:00	C7 **Tim Gould** (GU) *Trustworthy computational modelling for general chemistry*	
12:15	*End of session*	
12:15	**Lunch**	**Venue: Mezzanine Level (N76)**

Afternoon Programme

Afternoon Parallel Sessions		
	Medicinal Chemistry - Chair: Katarzyna Kepa	**Venue: Central Theatres (N18_Th2)**
1:40	A8 (S) **Caleb M T Kam** (BondU) *Design and synthesis of selective inhibitors for poly(ADP-ribose) polymerase member 14 (PARP14)*	
1:45	A9 (S) **Thanh Nguyen** (GU) *Identification of chemical probes against Parkinson's disease from Macleaya coradata*	
1:50	A10 (S) **Amanda Tauber** (BondU) *Design and synthesis of potential ARTD8 inhibitors towards the treatment of metastatic prostate cancer*	
1:55	A11 (S) **Eden Little** (GU) *Evaluation of natural products from traditional Chinese medicines against α-synuclein-targeted drug screening*	
2:00	A12 **Sara Motamen** (GU) *Discovery of ligand structure-activity relationship by mass spectrometry: identification of new tuberculosis inhibitors*	
2:15	A13 **Saleha Akter** (UQ/CSIRO) *Safety assessment of ellagic acid-rich extracts from Terminilia ferdinandiana*	
2:30	A14 **William Miao** (GU) *Discover chemical probes for Parkinson's disease from neuroprotective traditional Chinese medicines*	
2:45	A15 **Philip Ryan** (GU) *Design, synthesis and biological evaluation of bimodal glycopeptides as inhibitors of α-synuclein aggregation*	
3:00	*End of session*	

Afternoon Parallel Sessions cont.		
	Analytical, Food and Chemistry Education - Chair: Mary Fletcher	**Venue: Campus Heart N76_1.04**
1:40	B8 (S) **Paul Denman** (UQ) *Vitamin B12 as a reactive surface enhanced Raman probe for the quantification of sulphite*	
1:45	B9 (S) **Elvis T Chua** (UQ) *The ionic liquid cholinium argininate is an efficient solvent for extracting high-value Nannochloropsis sp. lipids*	
1:50	B10 (S) **Zoe Porter** (BondU) *HPLC-based methods used to determine whole cell sialic acid in biological samples*	
1:55	B11 (S) **Mahnaz Gholami** (QUT) *Optical sensors for detection of heavy metal pollutants in aqueous medium*	
2:00	B12 (S) **Shammy Sarwar** (UQ) *Physiochemical characteristics of commercial strawberries cultivars grown in Australia*	
2:05	B13 (S) **Eshetu M Bobasa** (UQ) *Native Australian fruits: freeze-dried Kakadu plums (Terminalia ferdinandiana) powder as an example for a high-quality food product*	
2:10	B14 **Michael Netzel** (UQ) *Strawberries : higher in folate than previously though*	
2:25	B15 **Marietjie Mostert** (UQ) *The application of ICP-OES spectroscopy to the accurate determination of phosphorus in matrix-dense rock solution*	
2:40	B16 **Hung T Hong** (UQ) *The effect of physiological maturity and different cooking methods on anthocyanin accumulation in purple sweetcorn kernels*	
2:55	*End of session*	
	Inorganic, Organic and Theoretical Chemistry - Chair: Romain Lepage	**Venue: Campus Heart N76_1.05**
1:40	C8 (S) **Julia L Kurz** (UQ) *Ketol-acid reductoisomerase (KARI) inhibitors as potential anti-tuberculosis prodrugs*	
1:45	C9 (S) **Eric Boittier** (UQ) *Development of computational tools for the design of heparin/glycosaminoglycan mimetics*	
1:50	C10 (S) **Ras B Roseli** (UQ) *TD-DFT investigation of the ESIPT mechanism of optoelectronic materials*	
1:55	C11 (S) **Alicia Kirk** (UQ) *Recycling organophosphorus catalysts for greener chemistry: computational studies into the mechanism of phosphine oxide reduction by organosilanes*	
2:00	C12 **Luke Churchman** (UQ) *Synthesis of intermediates in steroidal saponin biosynthesis*	
2:15	C13 **Jack Everson** (GU) *An unexpected outcome from a Horner-Wadsworth-Emmons reaction*	
2:30	C14 **Andrew Pearson** (GU) *Breaking Bad: a proactive approach to enhance the transition, engagement and confidence of health students in chemistry*	
2:45	C15 **Leon Burgess-Dean** *Nano-chemistry of CalaAlSil porous polysilicates and natural polymers composites*	
3:00	*End of session*	
3:00	**Afternoon tea**	**Venue: Mezzanine Level (N76)**

Afternoon Plenary Session - Chair: Mark Coster		**Venue: Central Theatres (N18_Th2)**
3:45	**Plenary lecture P3: Professor Francesco Peri** – University of Milano-Bicocca – *Synthetic glycolipids targeting Toll-like Receptor 4: new therapeutic perspectives*	
4:30	Presentation of Prizes for Contributed Talks and Short Presentations and Closing Remarks	
5:00	**The symposium will be followed by a social gathering to stimulate further networking opportunities at the UniBar**	

Key:
GU – Griffith University
QUT – Queensland University of Technology
UQ – University of Queensland
BondU – Bond University
QH – Queensland Health
CSIRO – Commonwealth Scientific and Industrial Research Organisation

P1 - Theoretical and computational molecular science: from non-equilibrium systems to materials for sustainable energy applications

Professor Debra Bernhardt

School of Chemistry & Molecular Biosciences, The University of Queensland, Brisbane, Australia

Australian Institute for Bioengineering and Nanotechnologies, The University of Queensland, Brisbane, Australia

Computational molecular science is increasingly being used to understand and predict the behaviour of systems at the molecular level. This is due to recent advances in algorithms, availability of software and greatly enhanced computer hardware. Due to these developments, it is often possible to model properties of systems where analytical relationships do not exist or the system is very complicated. However, limitations on timescale and lengthscale remain problematic. Furthermore, for some systems including non-equilibrium systems, the fundamental theory is not fully developed. Improving knowledge of these systems opens opportunities to develop new fundamental relations and new algorithms. This would also further expand capabilities for modelling.
We are interested in problems spanning a broad range of theoretical and computational molecular science. One area of research focus is the practical application of computational molecular science to sustainable energy technologies. Another is the development of the theory of non-equilibrium systems. In this talk I will discuss an example of work we have carried out in each of these areas.

P2 - Controlling Bacterial Biofilms with Nitroxides

Kathryn E. Fairfull-Smith*

Faculty of Science and Engineering, Queensland University of Technology, Queensland 4001, Australia

k.fairfull-smith@qut.edu.au

The adhesion of bacteria to surfaces and their subsequent ability to aggregate into colonies called biofilms is a significant global problem in numerous applications, particularly as biofilms display an inherent resistance to antimicrobial agents. Low concentrations of the diatomic free radical nitric oxide has been shown to disperse bacterial biofilms to free swimming planktonic bacteria,[1] which has led to the development of coatings that release nitric oxide. However, the non-systemic delivery of gaseous nitric oxide remains challenging as nitric oxide is an extremely reactive molecule with a very short half-life. As an improved strategy, we have recently shown that nitroxides (persistent and stable free radial species that are sterically hindered versions of nitric oxide) can inhibit bacterial biofilm formation and disperse existing biofilms.[2] This presentation will discuss these results and detail our current work towards the design and development of novel nitroxide-containing anti-biofilm agents and materials.

1. N. Barraud, D. J. Hassett, S. Hwang, S. Kjelleberg and J. S. Webb, *Journal of Bacteriology*, **2006**, *188*, 7344-7353.
2. C. de la Fuente-Núñez, F. Reffuveille, K. E. Fairfull-Smith and R. E. W. Hancock, *Antimicrobial Agents and Chemotherapy*, **2013**, *57*, 4877-4881.

P3 - Synthetic glycolipids targeting Toll-like Receptor 4: new therapeutic perspectives

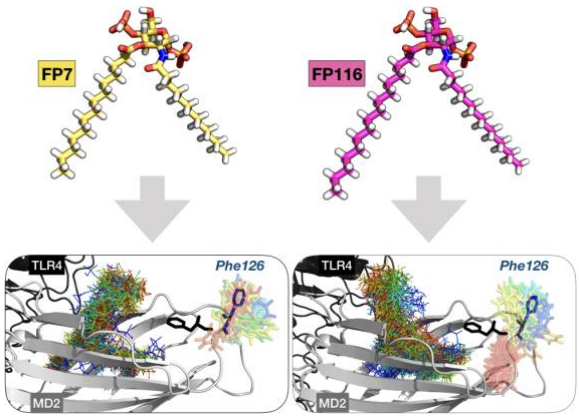
Francesco Peri,[1] Fabio Facchini, Florent Cochet, Andrea Luraghi, Valentina Artusa

E-mail: francesco.peri@unimib.it

[1] *Department of Biotechnology and Biosciences , University of Milano-Bicocca, Milano, Italy*

Toll-like Receptor 4 (TLR4) activation by pathogen-associated molecular patterns (PAMPs) or endogenous danger-associated molecular patterns (DAMPs) and subsequent cytokine production are the molecular events associated to several infectious and inflammatory diseases (including sepsis, viral infections, vascular inflammations, autoimmune and neurodegenerative diseases such as rheumatoid arthritis, amyotrophic lateral sclerosis and Alzheimer disease). Specific Toll-like Receptor 4 (TLR4) modulation (inhibition) by small molecular antagonists is considered a new approach to treat TLR4-related pathologies. On the other hand, TLR4 stimulation by agonists is considered a powerful and still poorly explored therapeutic option in tumor therapy and in the development of vaccine adjuvants. In this lecture, the most recent achievements in the rational design, synthesis, and biological characterization of new TLR4 modulators based on the structures of anionic and cationic amphiphiles, are reported and discussed. In the frame of the MSCA-ETN European project TOLLerant (www.tollerant.eu) we studied the capacity of synthetic compounds to modulate the TLR4 signal, in the perspective to develop new therapeutics targeting TLR4 [1].

Our synthetic molecules turned out to be good drug leads and their mechanism of action has been studied by binding studies with purified human MD-2 and murine and human cells expressing TLR4. A complete SAR study has been recently done on a group of synthetic glycolipids and will be discussed [2]. Preclinical data will be presented on the activity of the synthetic compounds on animal models of sepsis, influenza virus lethality [3], vascular inflammations [4], neuroinflammations [5], and inflammatory bowel disease (IBD).



[1] L. Zaffaroni, F. Peri Future Med. Chem. 2018, 10(4), 461-476.
[2] F.A. Facchini, et al. J. Med. Chem. 2018, (7), 2895-2909.
[3] L. Perrin-Cocon, et al. Sci. Rep. 2017, 7, 40791
[4] C. Huggins et al. Atherosclerosis 2015, 242, 563-570.
[5] M. De Paola et al. Pharm. Res. 2017, 103, 180-187.

A1 - Probing the Interactions of Amphiphilic Heparan Sulfate Mimetics with Heparanase

Vito Ferro*,[1] Mohit Chhabra,[1] Neha S. Gandhi,[2] Jennifer Wilson,[3] Norbert Wimmer,[1]

[1]School of Chemistry & Molecular Biosciences, The University of Queensland, Brisbane, Australia

[2]School of Mathematical Sciences and Institute for Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia

[3]School of Medical Science, Griffith University, Gold Coast Campus, Queensland, Australia

E-mail: v.ferro@uq.edu.au

PG545 (pixatimod), a heparan sulfate (HS) mimetic and anticancer agent [1] currently in phase I clinical trials [2], is a potent inhibitor of heparanase. The latter is an *endo*-β-glucuronidase that degrades HS in the extracellular matrix and basement membranes and is thus a key mediator of metastasis and angiogenesis. Herein, we report the improved synthesis of PG545 and several analogues with different aglycones, as well as approaches to labelled analogues for imaging studies. Furthermore, a conformational and molecular dynamics study of PG545 and selected analogues was carried out using the reported crystal structure of heparanase [3] in order to understand how PG545 interacts with this important drug target, and to guide the design of new inhibitors. These new compounds will aid in understanding the role of HS degrading enzymes in disease, especially cancer and inflammatory diseases, and will help elucidate the mechanism of action of PG545.

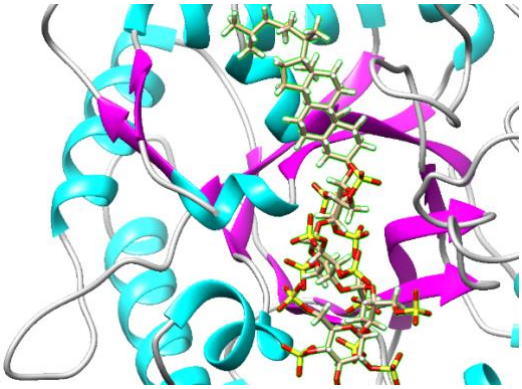


Figure: Heparanase in complex with PG545

References

1. Ferro, V.; Liu, L.; Johnstone, K. D.; Wimmer, N.; et al., *J. Med. Chem.* **2012**, *55*, 3804-3813
2. Dredge, K.; Brennan, T.V.; et al., *Br. J. Cancer*, **2018**, *118*, 1035-1041.
3. Wu, L., Viola, C.M., et al., *Nat. Struct. Mol. Biol.* **2015**, *22*, 1016–1022.

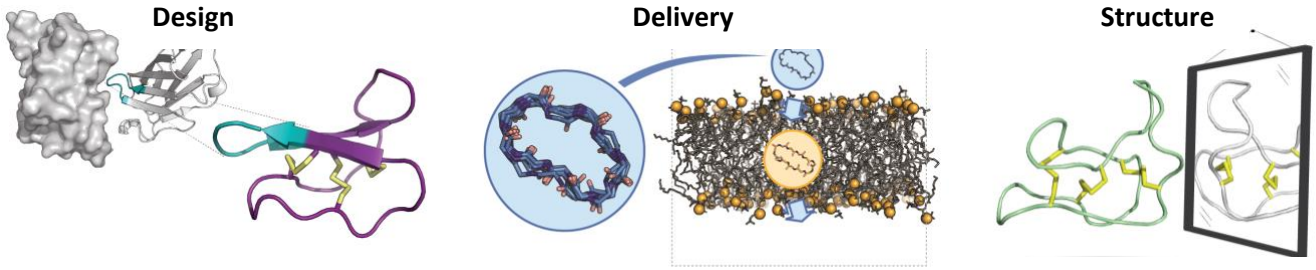
A2 - You better shape up, 'cause I need a drug

Conan K Wang*, David J Craik

Institute for Molecular Bioscience, The University of Queensland

c.wang@imb.uq.edu.au

My talk will be set on peptides, which are great drug leads because of their potential for high target affinity and selectivity. However, turning them into drugs has been a challenge. Here, I will focus on structure-based approaches for overcoming their limitations, enabling us to shape them into future drugs or diagnostics. The first limitation is poor metabolic stability, which can be overcome through geometric constraints to increase stability whilst preserving activity. I will discuss an approach akin to plant grafting, which involves fusing a bioactive peptide onto a highly rigid yet structure-enabling scaffold.[1] The approach has led to the design of stable peptides with activity observed in both *in vitro* and *in vivo* models of multiple sclerosis.[2] The second limitation is delivery and is perhaps more challenging. For instance, peptides are typically expected to have almost no oral bioavailability, making oral administration a difficult task, though there has been recent progress in the field. I will discuss how structures can help us address this challenge by understanding what makes certain peptides, like cyclosporin A, have high oral bioavailability,[3] which have led to the design of peptides with high oral absorption of ~30% in a rat model.[4] These examples constitute evidence of the importance of structural information in guiding peptide drug design and support the need to further investigate new methods for structure determination of peptides, which are currently underway. These advancements include the use of racemic mixtures to enable facile peptide crystallization[5] and limited NMR data to streamline the process of NMR structure determination. In all, I would like to emphasize the importance of structures in shaping the future of peptide design.



(1) Wang, C. K.; Craik, D. J. Designing Macrocyclic Disulfide-Rich Peptides for Biotechnological Applications. Nat Chem Biol 2018, 14, 417-427.

(2) Wang, C. K.; Gruber, C. W.; Cemazar, M.; Siatskas, C.; Tagore, P.; Payne, N.; Sun, G.; Wang, S.; Bernard, C. C.; Craik, D. J. Molecular Grafting onto a Stable Framework Yields Novel Cyclic Peptides for the Treatment of Multiple Sclerosis. ACS Chem Biol 2014, 9, 156-163.

(3) Wang, C. K.; Swedberg, J. E.; Harvey, P. J.; Kaas, Q.; Craik, D. J. Conformational Flexibility Is a Determinant of Permeability for Cyclosporin. J Phys Chem B 2018, 122, 2261-2276.

(4) Wang, C. K.; Northfield, S. E.; Colless, B.; Chaousis, S.; Hamernig, I.; Lohman, R. J.; Nielsen, D. S.; Schroeder, C. I.; Liras, S.; Price, D. A.et al. Rational Design and Synthesis of an Orally Bioavailable Peptide Guided by Nmr Amide Temperature Coefficients. Proc Natl Acad Sci U S A 2014, 111, 17504-17509.

(5) Wang, C. K.; King, G. J.; Northfield, S. E.; Ojeda, P. G.; Craik, D. J. Racemic and Quasi-Racemic X-Ray Structures of Cyclic Disulfide-Rich Peptide Drug Scaffolds. Angew Chem Int Ed Engl 2014, 53, 11236-11241.

A3 - Exploring the potential of endophytes and fungi as sources of anti-mycobacterial compounds

Jianying Han,[1] Ronald J Quinn,[1] Yunjiang Feng[1]

Griffith Institute for Drug Discovery, Griffith University, Brisbane, QLD 4111, Australia
jianying.han@griffithuni.edu.au

Tuberculosis caused by *Mycobacterium tuberculosis* is one of the most serious diseases, with an estimated 10.0 million new incident cases and 1.6 million people dying from this disease in 2017.

Microorganisms are one of the most important resources for providing prolific anti-TB natural products and drug leads, including clinically used drugs streptomycin, cycloserine, kanamycin, caperomycin and rifampicin. High throughput screening against *M. smegmatis* and *M. bovis* BCG strains gave 21 fungal and 7 endophytic extracts out of 350 extracts having activity against *M. smegmatis* with MIC value less than 400 μg/mL. 16 compounds have been isolated from these active extracts with 4 compounds showing activity against *M. smegmatis*.

Based on both the activity data and chemical analysis, 9 active strains were selected for co-cultivation to mimic the natural ecological situation. Preliminary results showed that the chemical profile of 17 out of 218 co-cultural extracts significantly changed during the interaction. These biological data and chemical profiles lay the foundation for all further active constitution study.

A4 - Glycolipid-based Nanostructures for Macrophage Targeted Antimicrobial Drug Delivery

Tamim Mosaiab*[1], Milton J. Kiefel[1], Todd A. Houston[1]
[1]Institute for Glycomics, Gold Coast Campus, Griffith University, QLD 4222
tamim.mosaiab@griffithuni.edu.au

Cell-surface glycoconjugates from *Mycobacterium tuberculosis* (TB) play important roles in immune evasion and pathogen survival within host macrophages. We have created a simple mimic of the TB phosphatidylinositol mannoside (PIM) core structure for use in antibiotic drug targeting. Preliminary results show these simple glycolipids limit cytokine production in activated macrophages.[1] We will report on our work to incorporate this PIM mimic into liposomes, micelles and nanoparticles to deliver antibiotics to macrophages selectively. Importantly, we have been able to incorporate both hydrophilic and hydrophobic drugs in the same formulation. With additional fluorescent cargo in such systems, we have shown enhanced uptake into phagocytic cells and improved antibacterial efficacy against intracellular *S. aureus*.[2]

[1] Mosaiab, T. M.; Boiteux, S.; Zulfiker, A. H. Md.; Wei, M. Q.; Kiefel, M. J.; Houston, T. A. *ChemBioChem* **2018**, *19*, 1476-1492.
[2] Sun, H.-K.; Pang, A.; Farr, D. C.; Mosaiab, T. M.; Britton, W. J.; Anoopkumar-Dukie, S.; Grice, I. D.; Kiefel, M. J.; West, N. P.; Grant, G. D.; Houston, T. A. *Aust. J. Chem.* **2018**, *71*, 716-719.

A5 - New flavonoids and saponins from *Gynostemma pentaphyllum* (Thunb.) Makino

Iftekhar Ahmed[1], David Leach[2,3], Hans Wohlmuth[2,3], Joanne Blanchfield[1] and James De Voss[1]

[1]School of Chemistry & Molecular Biosciences, The University of Queensland, St Lucia 4072, QLD, Australia
[2]Integria Healthcare, Logan Rd, Eight Mile Plains 4113 QLD Australia
[3]School of Health & Science, Western Sydney University, Locked Bag 1797, Penrith 2751 NSW, Australia
Corresponding author's email address: j.devoss@uq.edu.au

Gynostemma pentaphyllum (Thunb.) Makino has been the focus of extensive research over the past decade and this interest and popularity has led the Australian regulator, the Therapeutics Goods Administration (TGA), to call for compositional guidelines. There are no official monographs for this herb. The work undertaken and presented here encompasses composition of total flavonoids and saponins (the principal active constituents) in *G. pentaphyllum*.

Two new flavonoids (**1** & **8**) and five new triterpenoidal saponins (**14**, **15**, **19**, **22** & **23**), together with sixteen known compounds (**2-7**, **9-13**, **16-18** & **20-21**) were isolated from the methanol extract of the leaves of *G. pentaphyllum* and ethanol extract of ActivAMP (a heat treated commercial preparation of *G. pentaphyllum*). Their structures were elucidated on the basis of chemical and spectral methods, such as HSQC, HBMC, COSY, NOESY, 1D-TOCSY, UPLC and HRMS. A cell permeability assay, using Caco-2 cell model, on the isolated compounds was also performed to indicate the potential bioavailability of these compounds which can provide a better insight into the bioactivities of saponins and flavonoids from *G. pentaphyllum*.

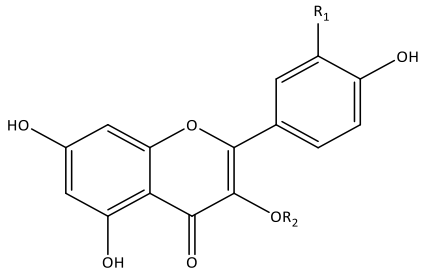


Figure 1: Flavonoids isolated form *G. pentaphyllum*

Flavonoids	R_1	R_2
1. kaempferol-3-O-α-rhamnopyranosyl -(1→2)-β-galactopyranoside	H	rhamnose-galactose
2. kaempferol 3-neohesperidoside	H	rhamnose-glucose
3. rutin	OH	rhamnose-glucose
4. isoquercitrin	OH	glucose
5. quercetin-3-O-α-rhamnopyranosyl-(1→2)-α-rhamnopyranosyl-(1→6)-β-glucopyranoside	OH	rhamnose-rhamnose-glucose
6. kaempferol-3-O-dirhamnogalactoside	H	rhamnose-rhamnose-galactose
7. kaempferol-3-O-dirhamnoglucoside	H	rhamnose-rhamnose-glucose
8. querctin-rhamnogalactoside	OH	rhamnose-galactose
9. querctin-rhamnoglucoside	OH	rhamnose-glucose
10. isorhamnetin rhamnogalactoside	OCH3	rhamnose-galactose
11. isorhamnetin rhamnoglucoside	OCH3	rhamnose-glucose

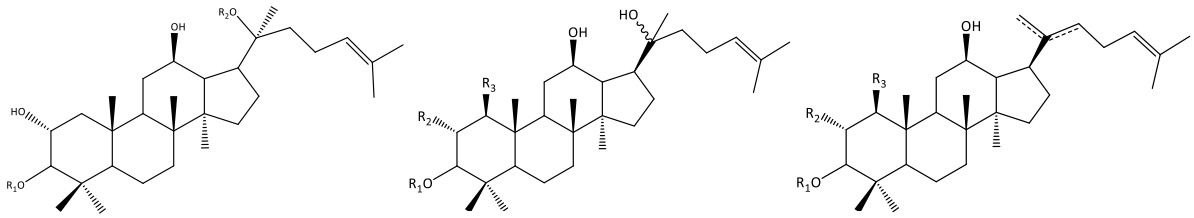


Figure 2: Saponins isolated form *G. pentaphyllum*

12. gypenoside LVI R_1=glc-glc, R_2 = glc-xyl
13. gypenoside XLVI , R_1=glc-glc, R_2 = glc
14. gypenoside LVI acetate R_1=glc-acetylglc, R_2 = glc-xyl
15. gypenoside XLVI acetate, R_1=glc-acetylglc, R_2 = glc
*glc= glucose, xyl= xylose

16. gypenoside L (20*S*), R_1= glc-glc, R_2 = OH, R_3 = H
17. gypenoside LI (20*R*), R_1= glc-glc, R_2 = OH, R_3 = H
18. yixinoside B (20*S*), R_1= glc-glc, R_2 = H, R_3 = OH
19. yixinoside B1 (20*R*), R_1= glc-glc, R_2 = H, R_3 = OH

20. damulin A $^{\Delta 20,22}$, R_1= glc-glc, R_2 = OH, R_3 = H
21. damulin B $^{\Delta 20,21}$, R_1= glc-glc, R_2 = OH, R_3 = H
22. damulin E $^{\Delta 20,22}$, R_1= glc-glc, R_2 = H, R_3 = OH
23. damulin F $^{\Delta 20,21}$, R_1= glc-glc, R_2 = H, R_3 = OH

A6 - Novel prodrugs against Mycobacterium tuberculosis Ketol-Acid Reductoisomerase (KARI)

Waleed M. Hussein, Ajit Kandale, Khushboo M. Patel, Nicholas P. West, Gerhard Schenk, Luke W. Guddat, Ross P. McGeary

School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, Australia
w.hussein@uq.edu.au

Tuberculosis (TB) is one of the major threats to global human health. There is an alarming increase in resistance to current medications against TB. The development of inhibitors of ketol-acid reductiosomerase (KARI) as novel anti-TB agents is a promising route to the treatment of this disease. In bacteria and plants KARI is a central enzyme in the biosynthetic pathway of the branched chain amino acids (i.e. leucine, isoleucine and valine), essential building blocks of virtually all proteins. Importantly, neither this pathway, nor the KARI enzyme, is present in animals. Thus, highly specific inhibitors of KARI and are not expected to be toxic to the human host. The activity of this pathway has been proven to be essential to the growth and survival of many bacteria, including *Mycobacterium tuberculosis* (Mt), the causative agent of TB. The aim of this project is to provide new classes of therapeutic drug leads to combat TB, and potentially other bacteria. One of the most effective ways to combat resistance is to develop new drugs that have new modes of action. In respect to resistance, KARI is a particularly interesting target since it has several immutable active site features (i.e. metal and NADPH binding sites) that if blocked should result in powerful inhibition. Thus, these compounds also have a low propensity to develop site-of-action resistance. Thus, the main hypothesis is that inhibitors of KARI can be developed into new drugs to prevent the growth of TB in infected humans.

A7 - Anti-TB Natural Products Identification Using Native Mass Spectrometry

Miaomiao Liu*, Angela Di Capua, Tin Mak, Ronald J Quinn

Griffith Institute for Drug Discovery, Griffith University, Australia
miaomiao.liu@griffith.edu.au

The TB epidemic is larger than previously thought with an estimated 10.4 million new TB cases worldwide in 2016. There were an estimated 1.3 million TB deaths and an estimated 490,000 new cases of multi-drug resistant TB (MDR-TB) in 2016. New drugs are essential to contribute to the "End TB strategy".

Nature Bank is a unique storehouse of nature's chemical diversity. It consists of over 63,000 biota samples of plants, and marine invertebrates sourced from tropical and temperature Australia, China and Papua New Guinea. A previous phenotypic HTS assay screening of the Nature Bank Fraction Library (202,983 fractions) against M. tuberculosis H37Rv resulted in 752 single point actives, 452 fractions, including 273 fractions form marine organisms showing a MIC following 11-point dose response analysis.

Modern drug discovery and development is heavily dependent on rapid and insightful analytical methods. Native screening using high resolution electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI-FT-ICR-MS) is a label-free, fast, accurate method that permits the direct observation of non-covalent protein-ligand complexes. The technique relies on non-denaturing electrospray-ionization (ESI) to firstly recognize multi-charged proteins in their near-native states.

This project enables the identification of a single natural product from a complex mixture by its specific interaction with TB proteins. The molecular weight mass information of the ligand allows identification of the active ligand in a pooled library. The simple mix and-measure, label-free nature of these experiments makes native ESI-FT-ICR-MS a practical technique to evaluate natural product binding.

B1 - Rapid bio-sensing of antibody drugs in human plasma

Saiqa Muneer[1], Emad Kiriakous[1], Godwin Ayoko[1]

[1]*School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology, Science and Engineering Faculty, 2 George Street, 4000, Australia*

Saiqa.muneer@hdr.qut.edu.au

The determination of antibody drugs is of fundamental importance to the therapeutic monitoring of these drugs. However, the current techniques such as HPLC-MS and ELISA are time consuming, expensive and lack the required sensitivity for accurate quantification of these drugs in biological fluids. Herein, we present a sensitive and selective Raman nano sensing methodology for the screening of Infliximab, a chimeric monoclonal antibody drug for autoimmune diseases, in human blood plasma in less than an hour. In this methodology, a target-specific extractor chip is synthesised and used for the selective extraction of the target antibody. The molecular structure of the purified antibody is then modified and directly loaded onto gold nano sensor and quantified by surface enhanced Raman spectroscopy down to 0.1 pM by a handheld Raman device. The new nano sensing method has strong potential for the point-of-care therapeutic monitoring of infliximab and can be easily extended to other antibody drugs such as Humira® (Adalimumab).

B2 – Investigation of salivary sialic acid as a biomarker in obesity: determination of both free and protein-bound sialic acids 5-*N*-acetylneuraminic (Neu5Ac) and 5-*N*-glycolylneuraminic (Neu5Gc) acids in human saliva

Hyo Jeong (Minnie) Kim*, Stephanie Scheweiker, Hayley O'Neill and Stephan Levonis

Bond University

h.kim@bond.edu.au

Sialic acids are a group of monosaccharides that are abundantly found in the mammalian cell surface. There is a strong correlation between serum sialic acids and various obesity-induced complications, however salivary sialic acids as a biomarker for obesity is a largely unexplored area.

A cost-effective method was developed using reverse-phase ion-pairing HPLC-UV using triisopropylamine as the ion-pairing agent with C18 column. Neu5Gc and Neu5Ac were eluted with the retention time of 5.33 min and 5.94 min respectively with a flow rate of 0.4 mL/min. For Neu5Ac, the recovery from spiking ranged from 79.9% to 109.9% with the limit of detection and limit of quantification calculated for Neu5Ac were 0.0353 mM and 0.1176 mM respectively.

The column efficiency is 6503 ± 95.22. With optimised method, a possible relationship between total salivary sialic acids level and obesity features such as BMI and fat mass vefore and after the weight loss was explored. Salivary samples were collected prior to and after the 30 weeks weight loss by calorie restriction from 15 obese women (preBMI: 94.2 kg/m^2, 79.9 – 127.7 kg/m^2, postBMI: 86.4 kg/m^2, 75.2 – 120.2 kg/m^2). There was no statistically significant difference in salivary sialic acids level between pre- and post-weight loss ($Z = -0.785$, $p = 0.433$) despite significant difference in BMI ($Z = -3.408$, $p = 0.001$). There was no statistically significant association between salivary sialic acids level and obesity features such as BMI ($r_{pre} = -0.108$, $p_{pre} = 0.713$; $r_{post} = -0.037$, $p_{post} = 0.899$) and fat masses as well ($r_{pre} = -0.051$, $p_{pre} = 0.863$; $r_{post} = 0.451$, $p_{post} = 0.106$). The findings from this project mmay add another viewpoint to previous studies where it was concluded that serum sialic acid level is associated with individual features of metabolic syndrome from obese individuals (Browning et al. 2004).

The work conducted successfully quantified the Neu5Ac levels in human saliva. The exploration of the relationship between sialic acid and obesity was attempted.

B3 - Indospicine residues in meat and liver from Western Australian cattle – a survey and risk assessment

Gabriele Netzel*[1], Mary Fletcher[1], Anne Masters[2], Jeremy Allen[2], Dieter Palmer[2]

[1]Queensland Alliance for Agriculture and Food Innovation (QAAFI), The University of Queensland, PO Box 156 Archerfield, 4108 QLD, Australia;

[2]Department of Primary Industries and Regional Development, South Perth, 6151 WA, Australia

g.netzel@uq.edu.au

Indospicine (L-2-amino-6-amidinohexanoic acid) is a natural hepatotoxin, which is only found in *Indigofera* plant species. These legumes are prevalent across northern Australia and are highly palatable to grazing cattle. Indospicine residues accumulate in cattle tissues and can persist for several months after exposure. Canine fatalities have occurred in Australia from the consumption of indospicine-contaminated horse and camel meat in the past. In this study, a survey was undertaken to assess whether the indospicine levels in meat samples collected from abattoirs in Western Australia are a risk for human consumption and may have an impact on trade and health. Muscle and corresponding liver samples from 776 cattle originating from Kimberley/Pilbara regions were collected at abattoirs across 4 seasons in 2015-2017, and analysed for indospicine residues.

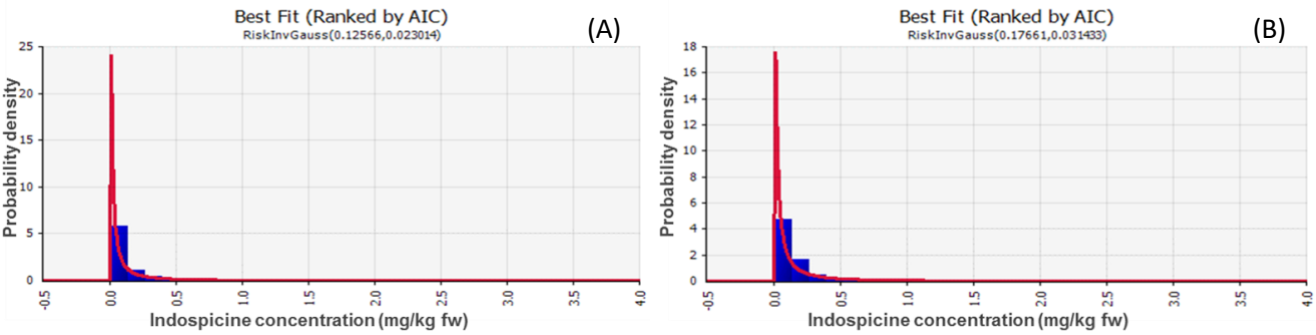


Fig. 1: Probability distributions of indospicine in all collected muscle (A) and liver (B) samples originating from Kimberley/Pilbara regions

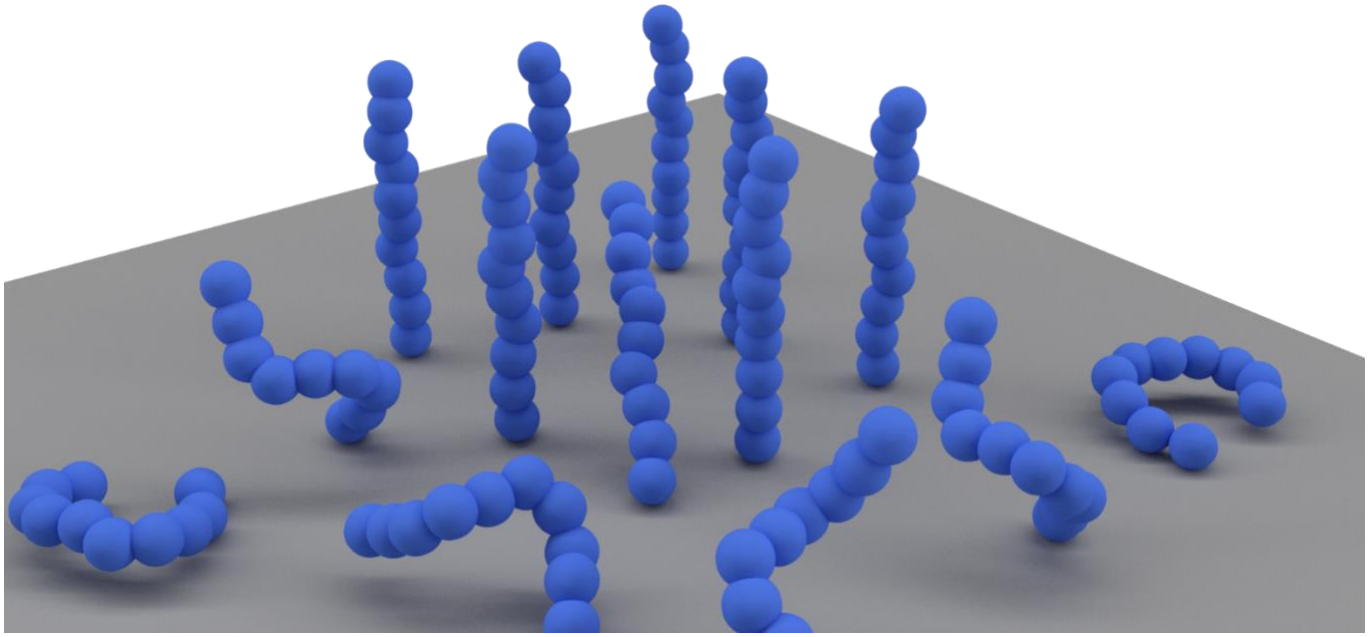
The indospicine prevalence was generally higher in Autumn, compared to Spring collections, with levels between below detection to 3.36 mg/kg. @Risk best-fit probability distributions showed ninety-fifth percentile (P95) indospicine concentrations of 0.54 mg/kg for muscle and 0.77 mg/kg for liver in this 2015-2017 period. Considering the average Australian daily meat consumption, the calculated estimated exposure for P95 muscle was 0.31 µg indospicine/kg bw/day, which compares favourably with our calculated provisional tolerable daily intake (PTDI) of 1.3 µg indospicine/kg bw/day. However, the estimated P95 canine exposure, which exceeds the calculated PTDI by a factor of 25, is of potential concern.

B4 - Exploring the Limits of Surface Grafting

Lukas Michalek,* Kai Mundsinger, Christopher Barner-Kowollik, Leonie Barner
School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology (QUT), 2 Gorge Street, Brisbane, QLD 4000, Australia

lukas.michalek@qut.edu.au

Polymers covalently attached to surfaces can exhibit different confirmations, primarily depending on the distance amongst tethering sites which is described by the grafting density σ.[1] For surface functionalization, two main methods can be employed, i.e. the 'grafting-to' and the 'grafting-from' approach. The latter method is generally suggested to lead to higher grafting densities as polymers are grown in-situ from the surface in a process driven by monomer diffusion. Nevertheless, the 'grafting-from' method suffers from information about the degree of polymerisation (DP) and molar mass distribution (MMD) of the grafted polymer.[2] A critical advantage of the 'grafting-to' approach is that the polymers can be characterized post-synthesis, prior to their surface attachment.[3]
In the current study, we explore the limits of surface grafting – of the 'grafting-to' approach – by conducting atomic force microscopy (AFM) based single-molecule force spectroscopy (SMFS) and size exclusion chromatography. The determined length of the polymer on the surface via SMFS is disparate than the expected length from the SEC traces. We discovered that grafting a distribution of polymer chains onto an interface critically affects the shape of the distribution, with shorter chains being preferentially attached.

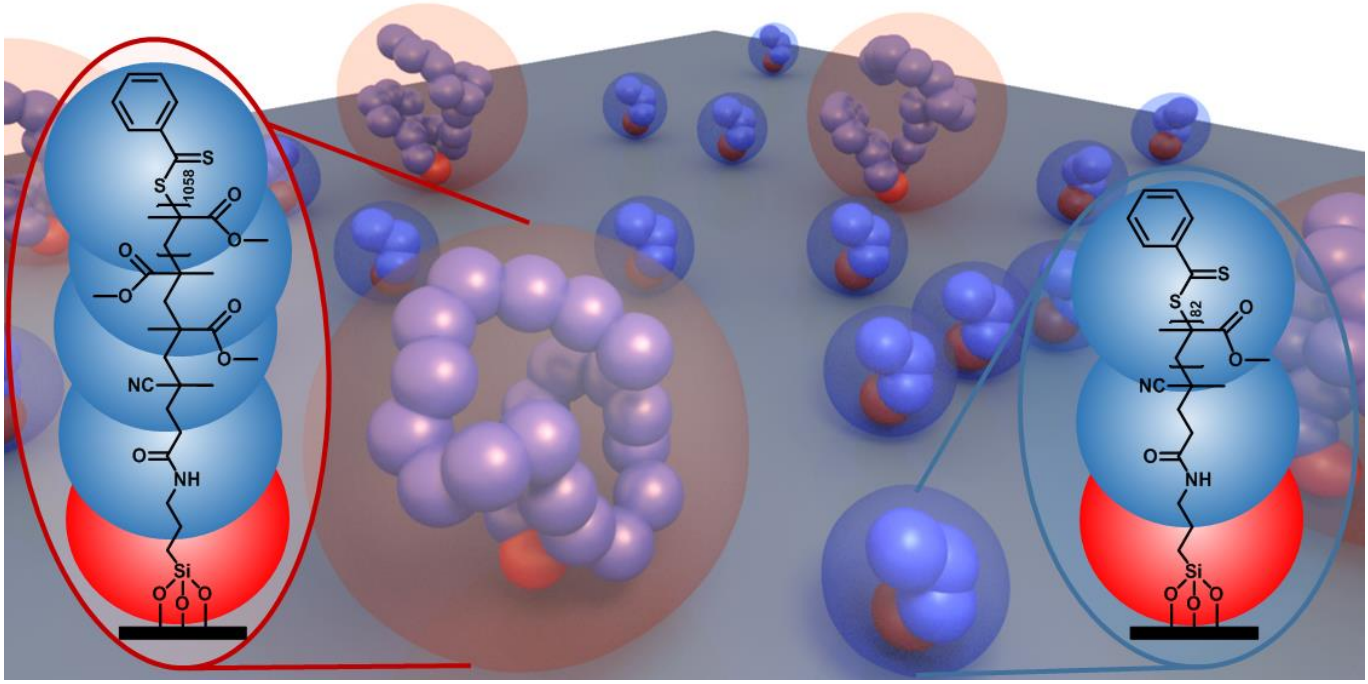


[1] L. Michalek, L. Barner, C. Barner-Kowollik, *Adv. Mater.* **2018**, 1706321.
[2] B. Zhao, W. J. Brittain, *Prog. Polym. Sci.* **2000**, *25*, 677-710
[3] M. Kim, S. Schmitt, J. Choi, J. Krutty, P. Gopalan, *Polymers* **2015**, *7*, 1346.

B5 - Understanding the Limits of Grafting-To

Kai Mundsinger,* Lukas Michalek, Leonie Barner, Christopher Barner-Kowollik
School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology (QUT), 2 Gorge Street, Brisbane, QLD 4000, Australia
k.mundsinger@qut.edu.au

Building upon previous findings, using atomic force microscopy we found a discrepancy of molar mass distributions grafted on surfaces compared to their polymers in solution, we further explore surface functionalization via grafting-to. Under the assumption that the polymer properties determined in solution accurately reflect the properties of the surface-tethered polymers, 'grafting-to' provides comprehensive knowledge about the functionalized surface.[1] However, this general assumption has never been experimentally tested and is questionable, as the preferential attachment of shorter over longer polymer chains appears likely due to differences in diffusion velocity and steric hindrance.[2] In the current study,[3] we scrutinize this hypothesis by conducting quartz crystal microbalance (QCM) measurements of surface grafted polymers and corroborate the results via Size Exclusion Chromatography (SEC) of polymer solutions used in surface grafting. We demonstrate that grafting a distribution of polymer chains onto an interface critically affects the shape of that distribution, with shorter chains being preferentially attached. This effect is herein quantified for the first time by grafting different poly(methyl methacrylate) (PMMA) distributions to silica surfaces. 'Grafting-to' of different ratios of number average molecular weight of PMMA distributions unambiguously illustrates the preferred surface grafting of shorter polymers, which can be correlated to their smaller radius of gyration. While grafting on QCM sensors allows to study the polymers grafted onto the surface it is limited to very low sample masses. Grafting polymers onto nanoparticles their high surface to volume ratio enables to work on a scale where classic solution methods like SEC can be applied. Our findings allow to establish a preferential grafting factor, κ, predicting the molar mass distribution of polymers on surfaces compared to the initial distribution in solution. Furthermore, SEC analysis enables characterization of solvent interactions in a straightforward manner using a very common instrument.



[1] B. Zhao, W. J. Brittain, *Prog. Polym. Sci.* **2000**, *25*, 677-710.
[2] H. Lizhong, N. Bernd, *Biotechnology Progress* **2003**, *19*, 544-548.
[3] L. Michalek, K. Mundsinger, C. Barner-Kowollik, L. Barner, **2018**, submitted.

B6 - Authentication of Australian honey (don't believe the headlines)

Sadia A Chowdhury[1,2], Shalona R. Anuj[1], James F Carter[1], Natasha L. Hungerford[2], Mary T. Fletcher[2]

[1] *Forensic and Scientific Services, Queensland Health, 39 Kessels Road, Coopers Plains*
[2]*QAAFI, The University of Queensland, 39 Kessels Road, Coopers Plains*
sadia.chowdhury@health.qld.gov.au

A joint ABC-Fairfax media investigation recently reported that testing at an international lab specialising in honey authentication found almost half of the 28 blended and imported honey samples selected from Australian supermarket shelves were "adulterated", meaning these honeys were believed to have been mixed with something other than nectar from bees. These allegations of adulteration have caused considerable industry and community concern, and the Australian honey industry is keen to reassure customers and demonstrate that Australian honey is safe and can be trusted.
The Official method of analysis AOAC 998.12 describes the carbon isotopic measurement of honey to determine the addition of C4 plant derived sugars such as cane sugar or high fructose corn syrup. This method measures the difference in carbon isotopic composition between the whole honey (preliminary sugar) and protein precipitated from the honey. A difference greater than 1 permilis is considered indicative of adulteration. Recent tests, however, in New Zealand found that a large proportion of Manuka Honeys failed this criteria, with the conversion of the bioactive dihydroxyacteone (DHA) to methylglyoxal (MGO) believed to be the key mechanism for the increase in the "apparent" C4 sugar content of Manuka honey. An alternative method specific to New Zealand honey has been proposed.

No equivalent research has been undertaken on Australian honey. The Australian honey bee industry is a small industry with a BIG impact. This research aims to establish the characteristics of Australian honey, and develop a honey analysis test that is fit for purpose, particularly where honeys derived from Australian Manuka (*Leptospermum* species) are concerned.

Reference:
Rogers, K. M.; Grainger, M.; Manley-Harris, M., The Unique Manuka Effect: Why New Zealand Manuka Honey Fails the AOAC 998.12 C-4 Sugar Method. *Journal of Agricultural and Food Chemistry* **2014**, *62*, 2615-2622.

B7 - Strategic Engagement of Foundation Year Health Students with Chemistry

Andrew Pearson*

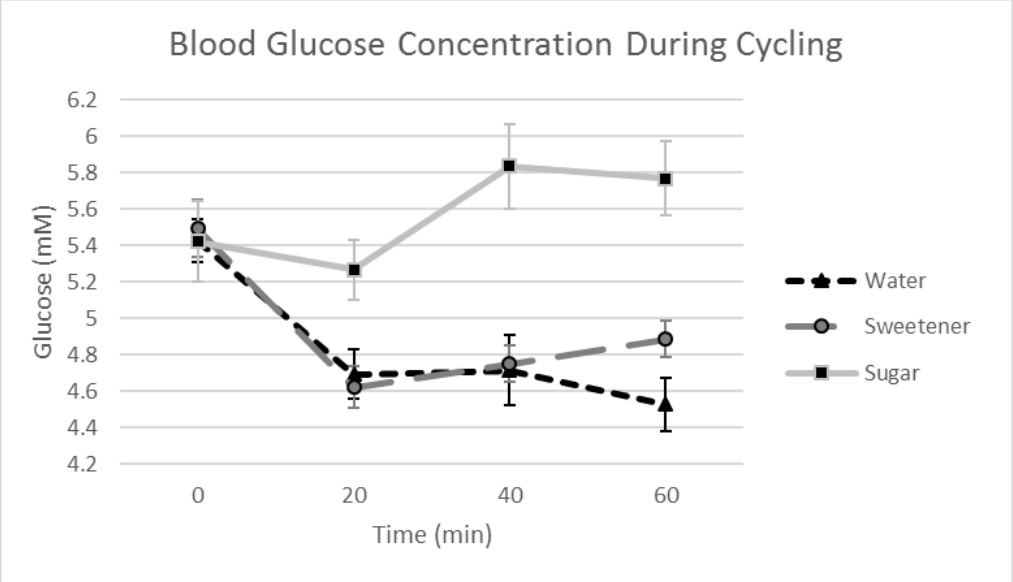
School of Medical Science, Griffith University, Gold Coast, Queensland, Australia

a.pearson@griffith.edu.au

Foundation Year Health students study introductory organic and biological chemistry through the study of functional groups and biological molecules. Although an effort is made to show the relevance of the content to students' future study and careers, many students still struggle to see the relevance and find the traditional approach to chemistry education difficult and/or uninspiring. An engagement strategy was developed to highlight the relevance of chemistry to a wide range of health professions. Activities were embedded into the curricula and designed around the chemistry of food, exercise and medicine.

This module has been delivered in a flipped mode, with videos presented on each of the three topics, followed by laboratory sessions. For the food laboratory, students cooked either a chicken or vegetable curry, learnt about spice compounds such as capsaicin and gingerol, then conducted a series of taste tests. For the exercise laboratory, blood glucose, triglycerides, and rating of perceived exertion were monitored while students cycled on a stationary bike for 60 min at a heart rate of 150 bpm and consumed either water, cordial with sugar, or cordial with sweetener. For the medicine laboratory, students learnt about origins of drugs, COX selectivity, diazepam metabolites, and binding to opioid receptors. Assessment was in the form of a laboratory workbook and questions on the final exam.

The module was evaluated through surveys and focus groups. Students reported the new module was engaging, relevant to their future careers, and helped them understand the application of organic and biological chemistry.



C1 - Glow Stick Chemistry – Making and Breaking Bonds with Chemiluminescence[1]

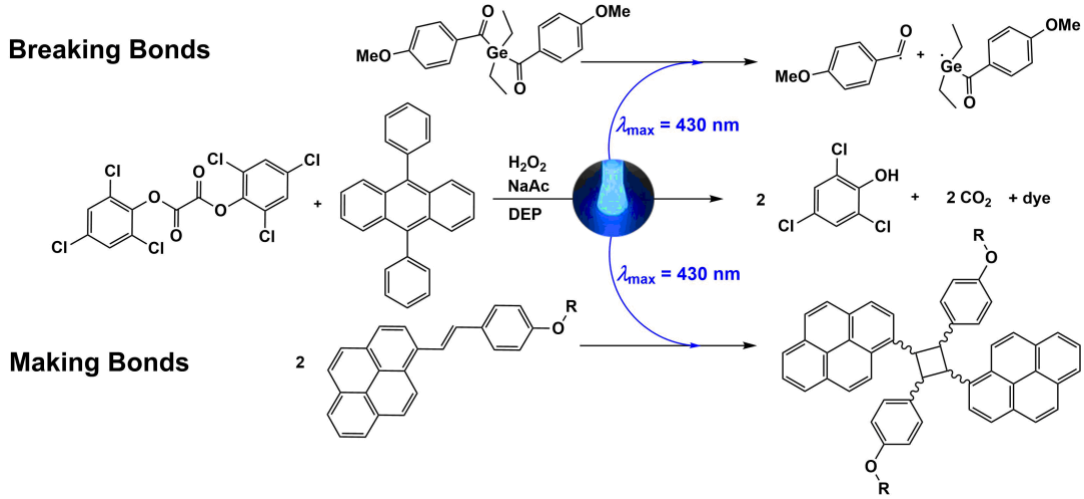
Katrin B. Kockler*†, Hendrik Frisch†, Christopher Barner-Kowollik†‡

†School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology, 2 George Street, Brisbane, QLD, 4000, Australia

‡Macromolecular Architectures, Institut fuer Technische Chemie und Polymerchemie, Engesserstrasse 18, 76131, Karlsruhe, Germany

Katrin.kockler@qut.edu.au

Chemiluminescence (CL) – the generation of light via chemical reactions – is a phenomenon widely observed in nature in the form of bioluminescence[2] and has inspired research throughout the centuries. Chemiluminescent reactions are powerful tools for chemical and medical analysis, including the detection of harmful substances in oils, water, or plant tissue,[3] and they are present in commercially available everyday objects such as glow sticks or emergency signalling devices. However, the potential of chemiluminescent light to trigger chemical reactions is scarcely investigated and has so far only been introduced to trigger oxidative cellular damage in photodynamic therapy in conjunction with a photosensitiser.[4] We demonstrate for the first time the usage of the low-intensity light of a chemiluminescent reaction to induce covalent bond breakage and formation. The generated photons enable both cleavage of species generating radicals as well as the execution of cycloadditions, demonstrating that disparate types of reactions can be triggered (Scheme 1).



The herein presented photochemical concept establishes the field of CL-induced photochemistry, which is poised to enable photochemical transformations in situations where the application of physical light sources, such as lamps, LEDs, or lasers is impractical, including for the intracellular generation of light in biological environments.

[1] K. B. Kockler, H. Frisch, C. Barner-Kowollik, *Macromol. Rapid. Commun*. **2018**, DOI: 10.1002/marc.201800516

[2] E. N. Harvey, *Bioluminescence*, Academic Press, New York **1952**.

[3] a) F. J. Pérez, S. Rubio, *Plant Growth Regul*. **2006**, *48*, 89; b) V. Stepanyan, A. Arnous, C. Petrakis, P. Kefalas, A. Calokerinos, *Talanta* **2005**, *65*, 1056;

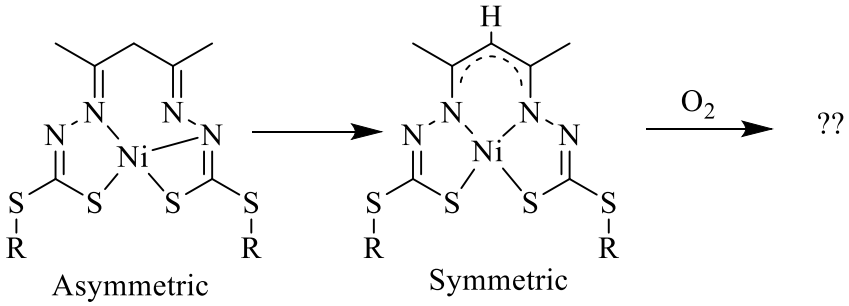
[4] R. C. M. C. Ferraz, C. Fontana, A. P de Ribeiro, F. Trindade, F. Bartoloni, W. Baader, E. Lins, V. Bagnato, C. Kurachi, *J. Photochem. Photobiol. B* **2011**, *103*, 87.

C2 - Nickel bis(dithiocarbazates): The Rebel Child of the *N*,*S* Chelating Family

Jessica K. Bilyj*, Paul V. Bernhardt
The University of Queensland
jessica.bilyj@uqconnect.edu.au

Dithiocarbazates, like thiosemicarbazones are renowned for their ability to stabilize high oxidation state transition metal complexes due to the balance of conjugation and charge delocalization found in the N-S chelate ring.[1] Work with nickel(II) bis(thiosemicarbazones) *in situ* has seen the formation of static linkage isomers under anaerobic conditions, forming two configurations in solution; symmetric and asymmetric. Exposure to oxygen selectively oxidises the symmetric isomer at the methine position on the ligand to a ketone over 24 hours without affecting the asymmetric isomer.

Investigating nickel bis(dithiocarbazates) has since shown that one cannot assume this family of complexes maintains the same chemistry in solution. *In situ* analysis under anaerobic conditions, specifically using ^{1}H NMR and cyclic voltammetry, has demonstrated a link between the linkage isomers (asymmetric and symmetric) by observing them as kinetic and thermodynamic products of one another respectively. In addition to this initial conversion, exposure to oxygen sees further reactivity commence.



R = methyl, benzoyl

1. Akbar Ali, M.; Bernhardt, P. V., Brax, M. A. H.; England, J.; Farlow, A. J.; Hanson, G. R.; Yeng, L. L.; Mirza, A. H.; Wieghardt, K. *Inorganic Chemistry*. **2013**, *52* (3), 1650-1657

C3 - Metallosupramolecular polyhedra for inclusion in multicomponent co-crystals

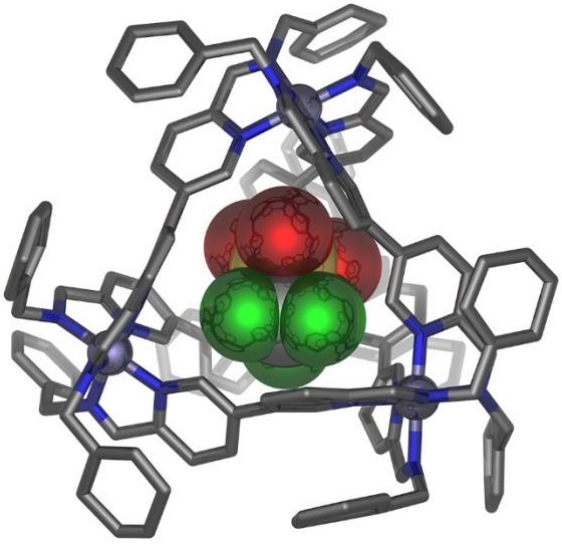
Marco Pandullo

Chemistry Department, E block, QUT Gardens Point

2 George St., Brisbane City, QLD, 4000

marco.pandullo@hdr.qut.edu.au

This project is concerned with the formation of novel metallosupramolecular cages, and their co-crystallization through halogen bonding as well as other non-covalent intermolecular interactions for manipulating the crystal packing of relatively bulky supramolecular polyhedra. This will provide a handle with which to tune the distance between metals, relative orientations in space and potentially their properties. The main goal is to investigate the potential of halogen bonding to form higher order metallosupramolecular networks. The results will lead to a better understanding of large cage-like complexes, how their geometries affect the supramolecular motifs in their crystals, and whether the principal properties of the co-crystals (solubility, chemical stability, magnetism, spin-crossover, fluorescence, etc.) can be altered when compared to pure crystals of discrete cages. The ultimate goal is to determine a new approach for the fine tuning of the properties of supramolecular crystalline materials, as well as to find better and more efficient ways to exploit the central cavity of metallosupramolecular cages for a variety of host/guest, halogen bonding and solid-state applications.



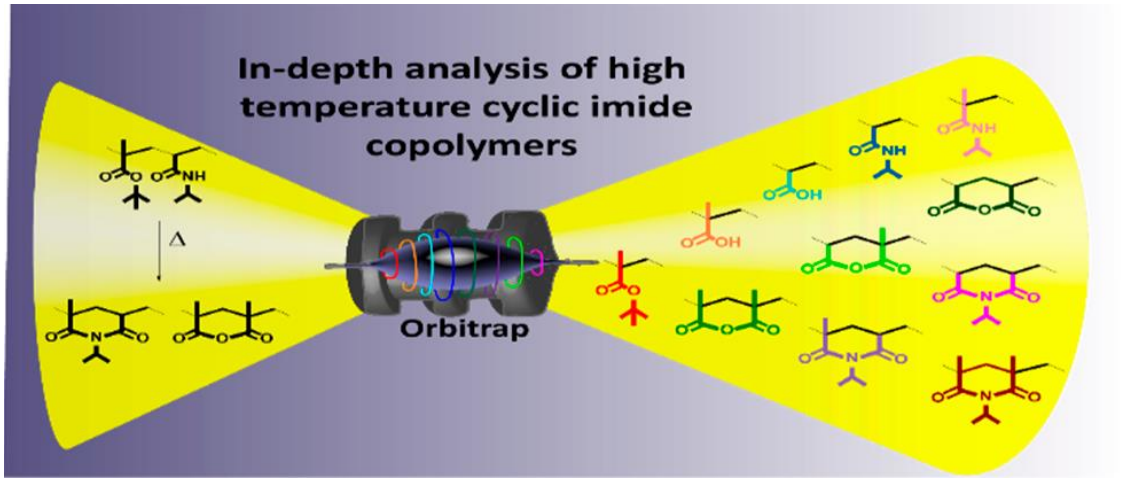
C4 - Correlating In-Depth Mechanistic Understanding with Mechanical Properties of High-Temperature Resistant Cyclic Imide Copolymers

Kristina J. Jovic*, Thomas Richter, Christiane Lang, James P. Blinco and Christopher Barner-Kowollik
School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology (QUT), 2 Gorge Street, Brisbane, QLD 4000, Australia

kristinajulia.jovic@hdr.qut.edu.au

Based on their outstanding properties polyimides have received an increased interest for applications as advanced materials. One specific class of polyimides are poly(methacrylimides) (PMI). PMIs can exceed a mechanical stiffness (Young's modulus) of greater than 6 GPa, a T_g close to 200 °C, and feature high-temperature resistance.

So far there exists no coherent mechanistic picture that unambiguously links the thermal and mechanical properties of the generated polymers with the molecular changes along the lateral polymer chain. Based on a copolymer of *tert*-butylmethacrylate (*t*-BMA) and *N*-isopropylacrylamide (NIPAM), we developed an in-depth mechanistic understanding of the molecular behaviour upon thermal treatment and were able to correlate this understanding with the mechanical properties of the resulting materials. Based on nuclear magnetic resonance (NMR), infrared (IR) spectroscopy, high-resolution mass spectrometry (HRMS) coupled to size-exclusion chromatography (SEC), tandem MS (MS/MS), thermogravimetric analysis (TGA) and nanoindentation, we correlate the time and temperature dependent cyclization process and optimize the system to achieve the highest T_g and *E*-modulus.



[1] Kristina J. Jovic, Thomas Richter, Christiane Lang, James P. Blinco and Christopher Barner-Kowollik, Macromolecules, 2018, in press

C5 - Small Molecular Hole Transporting Materials For Inverted Perovskite Solar Cells

Hong Duc Pham,[a] Hongwei Hu,[b] Krishna Feron,[c,d] Sergei Manzhos,[e] Hongxia Wang,[a] Nunzio Motta,[a] Yeng Ming Lam,[b] Prashant Sonar[a]

[a]*Institute of Future Environment and School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology (QUT), 2 George Street, Brisbane, QLD-4001, Australia.*
[b]*School of Materials Science and Engineering, Nanyang Technological University, 50 Nanyang Avenue, 639798, Singapore.*
[c]*Centre for Organic Electronics, University of Newcastle, Callaghan, NSW 2308, Australia.*
[d]*CSIRO Energy Centre, NSW-2304, Australia.*
[e]*Department of Mechanical Engineering, Faculty of Engineering, National University of Singapore, Block EA #07-08, 9 Engineering Drive 1, Singapore 117576.*
hongduc.pham@hdr.qut.edu.au
sonar.prashant@qut.edu.au

To date, perovskite solar cells (PSCs) have gained a big attention in the solar cell community due to the power conversion efficiency (PCE) increased quickly to world record 23.3% after the first achieved PCE of 3.8% in 2009.[1] However, the stability of the devices is still a significant issue. A lot of researches have been conducted to cope with this problem. Apart from them, the studies related to the synthesis of new organic semiconductors for hole transporting layer (HTL), where the extraction of photogenerated holes from the perovskite takes place and then these positive chargers are transported to the back contact metal electrode, play a key role in reaching the high stability and enhancing the PCE as well.[2] Indeed, the HTL protects the active perovskite layer from moisture/oxygen ingress and electrode penetration.[3, 4] In addition to the above benefits, the HTL suppresses charge recombination, which is critical for achieving higher PCE.[3] The HTL is essential to achieve higher open circuit voltage (V_{oc}) and PCE in the inverted (p-i-n) PSCs.[5]

In the chemistry view, organic hole transporting materials (HTMs) can be classified into two main categories: small molecules and polymers. Currently, the highest PCE obtained with inverted PSCs was around 19.4% using poly[bis(4-phenyl)(2,4,6-trimethylphenyl)amine] (PTAA) as the HTM.[6] Additionally, poly(3,4-ethylenedioxythiophene : polystyrene sulfonate) (PEDOT : PSS) has been also successfully used as the HTM in p-i-n devices and was able to achieve a high PCE of 18.1%.[7] Using these polymeric HTMs, it has been shown that it is possible for p-i-n devices to obtain PCE values that are comparable to those of conventional n-i-p structures. However, these most successful polymeric HTMs have some limitations when they come to practical applications in the PSCs technology. PTAA polymers are extremely expensive and costs about 50 times the price of gold and PEDOT:PSS ones are hydrophilic and a strong acidic nature which compromises the device long-term stability.[8] The tediousness of synthesis and the requirement of high purity of monomers may add to the cost of the polymers. Moreover, molecular weight of polymers can vary batch-to-batch and this may further affect the performance of PSC. Compared to polymeric semiconductors as HTMs, small molecular ones can provide enormous benefits including good yield,[9] defined molecular structure,[10] tunable energetics,[11] and good batch-to-batch reproducibility.[9, 10] Therefore, these bottlenecks of polymeric HTMs can be coped with by developing new small molecular HTMs via rational molecular design.

C6 - Scalable Production of Graphene Oxide via 3D-Printed Packed-Bed Electrochemical Reactor with Boron-doped Diamond Anode

Yu Lin Zhong *, Sean E. Lowe, Huijun Zhao

Centre for Clean Environment and Energy, School of Environment and Science, Gold Coast Campus, Griffith University, Gold Coast, QLD 4222, Australia

y.zhong@griffith.edu.au

Although graphene oxide (GO) has shown enduring popularity in the research community, its synthesis remains cost prohibitive for many of its demonstrated applications. Electrochemically produced graphene oxide (EGO) could potentially overcome some of these issues. While significant progress has been made on developing an electrochemical route to GO, existing methods have key limitations regarding their cost and scalability. To overcome these challenges, we employ a highly robust boron-doped diamond (BDD) with wide electrochemical potential window and commercially-available fused-filament 3D printing to design and optimize a scalable packed-bed electrochemical reactor for EGO production. This reactor is capable of producing EGO on a multiple-gram scale and is likely to be an order of magnitude cheaper than the current state-of-the-art Hummers-method GO process. By using flake graphite directly in our reactor with 11.6 M sulfuric acid as electrolyte, we have streamlined the production of EGO to a one-step electrochemical reaction step followed by a simple water wash purification. Almost all of the converted starting material can be recovered, and the final mass yield is typically 150% of the starting graphite material. The as-produced EGO is dispersible in water and other polar organic solvents (e.g. ethanol and DMF) and can be exfoliated down to predominantly single layer graphene oxide. We systematically demonstrate the scalability of the reactor along the vertical and lateral dimensions to facilitate its eventual industrial application. The EGO can be easily deoxygenated with low temperature thermal annealing (< 200 °C) to be converted into thermally converted EGO (TC-EGO) with a significantly enhanced conductivity. The degree of deoxygenation can be controlled via the thermal annealing time and the utility of such TC-EGO as a conductive nanofiller in lithium ion battery cathodes was demonstrated.

[1] Tian, Z., Yu, P., Lowe, S. E., Pandolfo, A. G., Gengenbach, T. R., Nairn, K. M., Song, J., Wang, X., Zhong, Y. L., Li, D. Facile Electrochemical Approach for the Production of Graphite Oxide with Tunable Chemistry. Carbon 112, 185-191 (2017).

[2] Yu, P., Tian, Z., Lowe, S. E., Song, J., Ma, Z., Wang, X., Han, Z., Bao, Q., Simon, G. P., Li, D., Zhong, Y. L., Mechanically-Assisted Electrochemical Production of Graphene Oxide. Chem. Mater. 28, 8429-8438 (2016).

[3] Lowe, S. E. & Zhong, Y. L., Chapter 13: Challenges of Industrial-Scale Graphene Oxide Production, Graphene Oxide: Fundamentals and Applications (ed. A. Dimiev & S. Eigler), John Wiley & Sons, Ltd., United Kingdom, 2016, ISBN: 978-1-119-06940-9.

[4] Yu, P., Lowe, S. E., Simon, G. P. & Zhong, Y. L, Electrochemical Exfoliation of Graphite and Production of Functional Graphene. Curr. Opin. Colloid Interface Sci. 20, 329 (2015).

C7 - Trustworthy computational modelling for general chemistry

Tim Gould*, Sherif Tawfik

QLD Micro- and Nanotechnology Centre, Nathan campus, Griffith University, 170 Kessels Road QLD 4111, Australia

t.gould@griffith.edu.au

The last decade has seen the development of hundreds of approaches to quantum chemistry, most based on density functional approximations. But this diversity brings with it a cost: it is difficult to know which method to choose. On the one hand, this can lead to (over)reliance on "old favourites", such as B3LYP, PBE or M06L, which can perform quite poorly in some circumstances. On the other hand, it can lead to (ab)use of "shiny new toys", which may not be appropriate for the problem at hand. There is an urgent need to assess which methods are reliable for general chemical problems, so that users can choose methods that will consistently yield trustworthy calculations in almost all instances.

Broad benchmarking, as exemplified by the GMTKN55[1] and MGCDB84[2] sets of thousands of systems are an important first step towards such an assessment. Both incorporate difficult physics such as delocalisation errors and dispersion forces, which general-purpose methods must get right. But despite their breadth, these sets neglect an important class of chemical problems – material (solid state) and surface chemistry. This talk will cover some of the challenges (e.g., Figure 1) in developing a general chemistry protocol, and highlight recent advances aimed at establishing and refining a solution to this difficult problem [3-5]. Ultimately, such a protocol will lead to better understanding of chemical problems as diverse as biochemistry, catalysis and filtration.

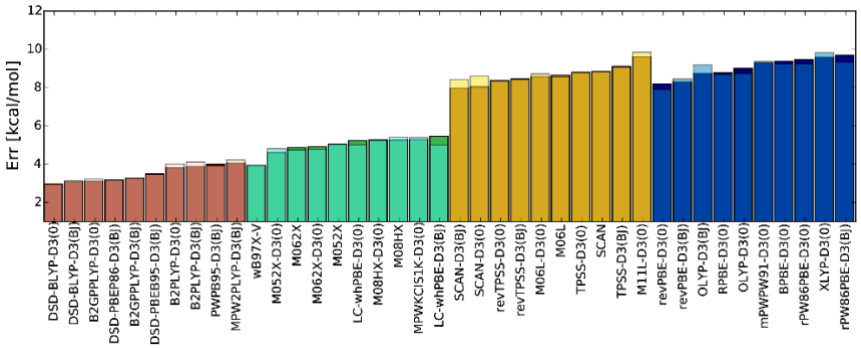


Figure 1: A general chemistry protocol will require accurate benchmarking of molecules using moderate numbers of samples, so it can be paired with small numbers of solid state samples. Results of a 'diet' protocol (clear) are compared here with GMTKN55 (solid), which illustrates that it is possible to reduce a large set to a small one with minimal loss of accuracy[4].

References:

[1] L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi and S. Grimme, *Phys. Chem. Chem. Phys.* **2017**, *19*, 32184–32215

[2] N. Mardirossian and M. Head-Gordon, *Mol. Phys.* **2017**, *115*, 2315–2372

[3] S. Tawfik, Tim Gould, Catherine Stampfl, and Michael J. Ford, *Phys. Rev. Mat.* **2018**, *2*, 034005

[4] T. Gould, *Phys. Chem. Chem. Phys.* Just accepted (2018)

A8 - Design and Synthesis of Selective Inhibitors for Poly(ADP-ribose) polymerase Member 14 (PARP14)

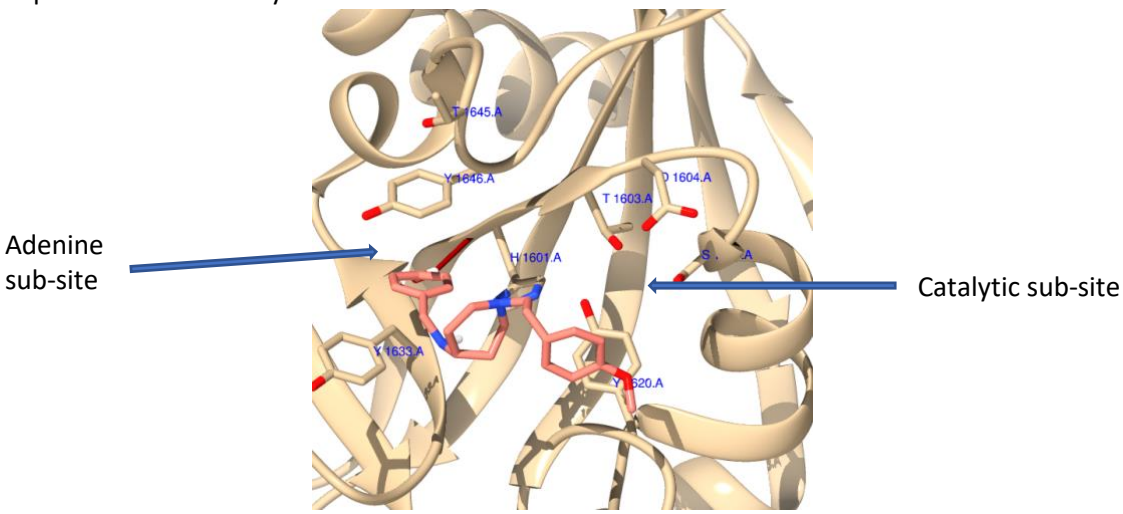
Caleb M.T. Kam*, Stephan M. Levonis **, Stephanie S. Schweiker

Medicinal Chemistry Department, Faculty of Health Sciences and Medicine, Bond University, Robina QLD 4229

*ckam@bond.edu.au *; slevonis@bond.edu.au ***

Prostate Cancer (PCa) is the second most commonly diagnosed cancer for men in western countries, and it is one of the most deadly cancers globally (1). Late stage PCa is highly aggressive and has the potential to spread throughout the body, limiting the treatment options. The poly (ADP-Ribose) polymerase, or PARP, is a superfamily of enzymes which are found in eukaryotic cells and modify histones and other nuclear proteins that are responsible for the survival of damaged, proliferating cells via poly(ADP-ribosyl)ation (2). PARP14 was found to be moderately overexpressed in PCa and some other cancers, and has been found to promote the Warburg effect and DNA repair mechanisms, aiding cell survival. Inhibition of PARP14 could potentially increase the efficacy of current oncotherapies (3).

Nine compounds were designed to potentially inhibit PARP14. The compounds were designed and computationally analysed using PyRx and Chimera. Key binding residues in PARP14 include His1601, Tyr1620, Tyr1633 and Tyr1640 (3SMI.pdb). All nine compounds displayed favourable binding affinities and key interactions that may help with selectively targeting PARP14 over the other PARP superfamily enzymes. The nine compounds were synthesised and characterised prior to PARP14 enzyme inhibition studies.



4-(((1-(4-methoxyphenethyl)piperidin-4-yl)amino)methyl)phenol docked to 3SMI.pdb, demonstrating a hydrogen interaction to PHE1600 with a binding affinity of -7.6kcal/mol *in silico*.

1. Hudson BD, Kulp KS, Loots GG. Prostate cancer invasion and metastasis: insights from mining genomic data. *Brief Funct Genomics.* **2013**;12(5):397-410.
2. Ame JC, Spenlehauer C, de Murcia G. The PARP superfamily. *Bioessays*. **2004**;26(8):882-93.
3. Weil MK, Chen AP. PARP inhibitor treatment in ovarian and breast cancer. *Curr Probl Cancer*. **2011**;35(1):7-50.

A9 - Identification of Chemical Probes against Parkinson's Disease from *Macleaya cordata*

Thanh D. Nguyen*, George D. Mellick, Yunjiang Feng
Griffith Institute for Drug Discovery, Griffith University
thanh.nguyen4@griffithuni.edu.au

The lack of our understanding about Parkinson's Disease (PD), the second most common and incurable neural degenerative disorder, has caused a great impact in both treatment and research for this disease. It is undeniable that not a few studies and efforts have been carried out with the hope of gaining more knowledge about the complex biology underlying this debilitating condition, yet it seems that the aetiology, and more importantly, the direct targets of this disorder remain mysterious.[1]

Cytological profiling, a phenotypic assay, has recently become a powerful unbiased strategy to study the molecular mechanisms in many biological systems, with one milestone being that this method was used to identify the mechanism of action of an antibacterial compound.[2] Previous studies utilizing cytological profiling at Griffith Institute for Drug Discovery have also identified quite a few compounds that could interact with PD patient-derived cell lines.[3] Constituently, it is worth believing that this technique could be a future approach for combating PD.

As part of our ongoing research intending to identify anti-PD molecules from nature, the species *Macleaya cordata*, a Traditional Chinese Medicinal plant, was selected for chemical investigation, resulting in the isolation of one new compound, 10-methoxybocconoline, together with eleven known alkaloids and five known polyphenols, the structures of which were extensively elucidated by 1D and 2D NMR spectroscopy, as well as mass spectrometry. These compounds will subsequently be analysed for bioactivities using the above-mentioned cytological profiling assay, evaluating the interactions between them and the cellular components to identify chemical probes for PD research.

1. Wang C, *et al.*; *ACS Chem. Neurosci.* **2016**, *7(12)*, 1628-1634. (b) Narayan P, *et al.*; *Nat. Chem. Biol.* **2014**, *10(11)*, 911-920
2. Nonejuie P, *et al.*; *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110(40)*, 16169-16174
3. Grkovic T, *et al.*; *Angew. Chem., Int. Ed. Engl.* **2014**, *53(24)*, 6070-6074. (b) Vial M, *et al.*; *J. Nat. Prod.* **2016**, *79(8)*, 1982-1989. (c) Wang D, *et al.*; *J. Nat. Prod.* **2016**, *79(2)*, 353-361

A10 - Design and Synthesis of Potential ARTD8 inhibitors towards the treatment of Metastatic Prostate Cancer.

Amanda Tauber*, Stephanie S. Schweiker and Stephan M. Levonis

Medicinal Chemistry Group, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia.
atauber@bond.edu.au

Metastatic prostate cancer is currently the third leading cause of cancer related death in Australia, in part due to its increasing prevalence and lack of therapies able to overcome the androgen independent nature of the late stage disease. A potential target could be ADP-ribosyl transferase member 8 (ARTD8, aka. PARP14, CoaSt6, BAL2). Part of the 17-membered family of post-translational modifiers, ARTD8 has gained traction as a chemopreventive target due to the correlation between its expression and the pathogenesis of many metastatic cancers, including prostate (Bachmann et al., 2014). As of yet, there is no clinically available selective ARTD8 inhibitor.

Our research explores the design, synthesis and *in vitro* evaluation of nine ARTD8 inhibitors. Designed as a lengthened nicotinamide mimic with the intention of interacting with both the catalytic and adenine binding subsites of the ARTD8 catalytic domain. The proposed compounds were designed and docked using AutoDock Vina, observing that many of the compounds spanned across both subsites of the domain. These nine novel compounds were synthesised using reductive amination. Preliminary assay results of compounds **7, 8** and **9** displayed a 55% reduction in ARTD8 activity.

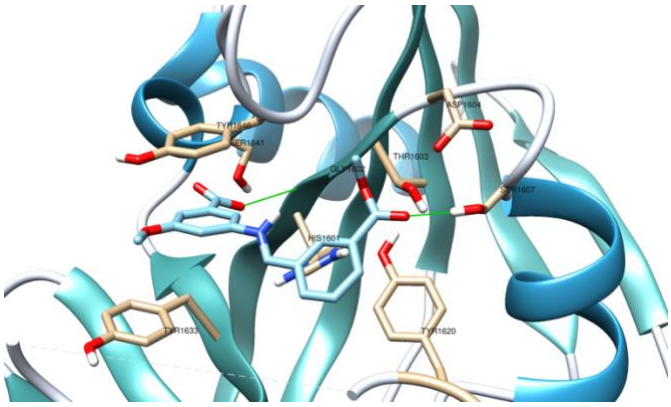


Figure 1: Compound 1 docked in to the catalytic domain of ARTD8 with key residues from both the adenine and catalytic subsites of the catalytic domain displayed (His1601, Gly1602, Thr1603, Asp1604, Ser1607, Tyr1620, Thr1632, Thr1633, Phe1634, Tyr1641, Tyr1645, Thr1646)

Bachmann, S. B., Frommel, S. C., Camicia, R., Winkler, H. C., Santoro, R., & Hassa, P. O. (2014). DTX3L and ARTD9 inhibit IRF1 expression and mediate in cooperation with ARTD8 survival and proliferation of metastatic prostate cancer cells. *Molecular Cancer, 13*(125).

A11 - Evaluation of bioactive natural products from traditional Chinese medicines against α-synuclein-targeted drug screening

Eden Little*, Stephen Wood, George Mellick, and Yunjiang Feng.

Griffith Institute for Drug Discovery, Griffith University

Eden.little@griffithuni.edu.au

Parkinson's Disease (PD) is the second most common neurodegenerative disorder which is classified as a cerebral amyloid disorder and common synucleinopathy.[1] Abnormal aggregations of the α-Synuclein protein found within nerve cells are a pathological feature of PD.[1] Therefore an important strategy in PD drug discovery is presented by potentially inhibiting the aggregation of α-Synuclein protein.

Over 100 natural products, derived from Traditional Chinese Medicine (TCM), were identified for their neuroprotective effects. These compounds demonstrated cytological profiles against several cell organelle functions which are believed to be causative of PD. Large scale isolation will be carried out on the targeted TCM compounds to isolate ~5 mg of each compound. The chemical structures of those are confirmed by comparison of exploratory 1D-, 2D- NMR and MS spectroscopic data to previous reported data within the literature. A high content cytological profile assay will profile the compounds for disease specific features via the utilisation of different cell lines. These selected compounds will then be further tested by a biophysical thioflavin T (Th T) assay, which quantifies the compounds binding affinities and demonstrates the compounds ability to prevent amyloid protein aggregation.

Natural products that display disease specific cytological profiles can then be used as a chemical probe to further investigate PD biology. The compounds that demonstrate inhibitory effects of protein aggregation can potentially be used as lead molecules for PD drug discovery.

[1]Mhyre, *et al.; Subcell Biochem.* **2012***, 65,* 389-455.

A12 - Discovery of Ligand Structure-activity Relationship by Mass Spectrometry: Identification of New Tuberculosis Inhibitors

Sara Motamen*, Yang Yang, Ronald J. Quinn

Griffith Institute for Drug Discovery, Griffith University, Brisbane, Australia
sara.motamen@griffithuni.edu.au

A set of tuberculosis fragment inhibitors has been discovered by mass spectrometry. The method is based on the observation of protein-ligand complexes by mass spectrometry.[1] These fragments may compete for common binding sites on the target protein or bind at different sites. Mass spectrometry enables identification of ternary complexes in which two ligands bind to different sites of a target.[2]

For a specific target, the result $(P+L_1) + (P+L_2)$ indicates binding to the same site (competitive), while the result $(P+L_1) + (P+L_2) + (P+L_1+L_2)$ shows that L_1 and L_2 bind to different sites (non-competitive). Compound design relies on using a number of competitive fragments linked to a non-competitive fragment. Therefore, the structures of these fragments will be modified using synthetic methods to enhance their activities and produce novel inhibitors.

1. Chan, Daniel S.-H.; Whitehouse, Andrew J.; Coyne, Anthony G.; Abell, C. Mass spectrometry for fragment screening. *Essays In Biochemistry* **2017**.
2. Pedro, L.; Quinn, R. J. Native mass spectrometry in fragment-based drug discovery. *Molecules* **2016,** *21* (8), 984.

A13 - Safety assessment of ellagic acid-rich extracts from *Terminalia ferdinandiana*

Saleha Akter [a, b*], Rama Addepalli [b], Michael E. Netzel [a], Ujang Tinggi [c], Mary T. Fletcher [a], Simone A. Osborne [b], Yasmina Sultanbawa[a]

[a] *Queensland Alliance for Agriculture and Food Innovation (QAAFI), The University of Queensland, Health and Food Sciences Precinct, 39 Kessels Rd, Coopers Plains, PO Box 156, Archerfield BC, Qld 4108, Australia*

[b] *CSIRO Agriculture and Food, 306 Carmody Road, St Lucia, QLD 4067, Australia*

[c] *Queensland Health Forensic and Scientific Services, Health and Food Sciences Precinct, 39 Kessels Rd, Coopers Plains, PO Box 594, Archerfield BC, Qld 4108, Australia*

*Presenting Author: Saleha Akter: saleha.akter@uq.edu.au

Terminalia ferdinandiana has a long history of nutritional and medicinal use by Indigenous Australians. Ellagic acid, a major component of *T. ferdinandiana*, is an antioxidant reported to provide therapeutic benefits against oxidative stress. We investigated the safety of ellagic acid-rich extracts of *T. ferdinandiana* by measuring *in vitro* viability of intestinal enterocytes (undifferentiated and differentiated Caco-2 cells), goblet cells (HT29-MTX-E12) and liver (Hep G2) cells in response to different extracts. Nine different dose points ranging from 33 to 200000 µg/ml were investigated using CyQUANT® NF Cell Proliferation Assay and CellTiter-Glo® Luminescent Cell Viability Assay to determine the number of metabolically active cells. Changes to cell viability produced IC_{50} values between 4415 and 12878 µg/ml for all of the extracts and cell lines tested in CyQUANT® NF Cell Proliferation Assay and between 3065 and 24765 µg/ml for all of the extracts and cell lines tested in CellTiter-Glo® Luminescent Cell Viability Assay. The IC_{50} values for standard ellagic acid varied from 1055 to 2244 µg/ml across the different cells and both assays. Undifferentiated (IC_{50} 1204 µg/ml, 3718 µg/ml) and differentiated Caco-2 cells (IC_{50} 1055 µg/ml, 3376 µg/ml) were the two most sensitive cell lines in both assays. The results of the present study indicate that ellagic acid-rich extracts of *T. ferdinandiana* improve cell viability *in vitro* compared to ellagic acid alone. Taken together, these results indicate that *T. ferdinandiana* extracts provide a safer option compared to therapeutic administration of ellagic acid.

A14 - Discover Chemical Probes for Parkinson's disease from Neuroprotective Traditional Chinese Medicines

William Miao*, Ron Quinn, and Yunjiang Feng

Griffith Institute for Drug Discovery, Griffith University, QLD
Williamgang.miao@griffith.edu.au

Traditional Chinese Medicine (TCM) plays an important part in healthcare in China and increasingly in western countries including Australia. However, the functions and mechanisms of TCMs have not been precisely researched which affect their acceptance by the regulatory authorizations in the western world. Many TCMs have neuroprotective effect against Parkinson's disease according to the traditional knowledges. One of the objectives of this project is to isolate the compounds from selected neuroprotective TCMs and to discover their therapeutic functions against cells from Parkinson's patients.

Gastrodia/Chuanxiong herbal pair is one of the TCM formulations that have been traditionally used for the treatment of neurodegenerative diseases, some of them are related the symptoms of Parkinson's disease. Gastrodia, Chuanxiong and their herbal pair were extracted using TCM traditional methods by hot water and ethanol, and modern natural product extraction method using hexane, dichloromethane and methanol accordingly. HPLC fractionation and ^{1}H-NMR testing of these extracts found traditional ethanol extraction is as effective as natural product extraction method, and quicker and greener.

90 compounds including five new compounds were isolated from the ethanol extracts of Gastrodia and Chuanxiong. The biological evaluation of these compounds as well as fractions and extracts of this herbal pair will be carried out against human olfactory neuron sphere cells (hONS cells) from Parkinson's disease patient, which includes cytological profiling assay and neuroprotective activity assay.

A15 - Design, synthesis and biological evaluation of bimodal glycopeptides as inhibitors of α-synuclein aggregation

Philip Ryan[1,2,3], Manny Xu[4], Andrew Davey[1,2,3], George Mellick[4], Santosh Rudrawar[1,2,3]*

[1] Menzies Health Institute Queensland, Griffith University, Gold Coast 4222, Australia
[2] School of Pharmacy and Pharmacology, Griffith University, Gold Coast 4222, Australia
[3] Quality Use of Medicines Network, Griffith University, Gold Coast 4222, Australia
[4] Griffith Institute for Drug Discovery, Griffith University, Nathan, 4111, Australia
**s.rudrawar@griffith.edu.au*

Located in the presynaptic terminals in neurons, the α-synuclein protein is a toxic, aggregating protein playing a major role in Parkinson's disease. Along with a number of self-assembling proteins involved in various neurodegenerative diseases, α-synuclein undergoes *N*-acetylglucosamine (GlcNAc) modification post-translationally. The modification occurs on Ser/Thr residues of thousands of proteins, altering their structure and function. Modification of α-synuclein with as little as one single *O*-GlcNAc unit has been shown to inhibit the proteins aggregation and alter its pathogenic processing.[1]

Available treatments for Parkinson's disease merely control the symptoms, there currently exists no therapy that can prevent progression of the disease. The majority of small molecules reported to bind α-synuclein also bind non-selectively to a variety of biomolecules. As such, they are burdened with a potential for inflicting numerous side-effects. Increasing a leads selectivity *via* structural optimisation is complicated by the nature of the aggregation process, characterised by unstable intermediate structural conformations and complexes arising throughout. Peptide-based strategies offer biologically active compounds that boast high selectivity due to their ability to establish multiple points of contact with their target.[2] Their strong, reversible binding also qualifies peptides as model *ex vivo* imaging agents. Here we have designed, synthesised and are in the process of evaluating a series of novel bimodal glycopeptides derived from the native α-synuclein sequence for their ability to inhibit pathological α-synuclein aggregation.

[1] N. P. Marotta, Y. H. Lin, Y. E. Lewis, M. R. Ambroso, B. W. Zaro, M. T. Roth, et al., *Nat Chem*, **2015**, *7*, 913.
[2] P. Ryan, B. Patel, V. Makwana, H. R. Jadhav, M. Kiefel, A. Davey, et al., *ACS Chemical Neuroscience*, **2018**, *9*, 1530.

B8 - Vitamin B12 as a Reactive Surface Enhanced Raman Probe for the Quantification of Sulphite

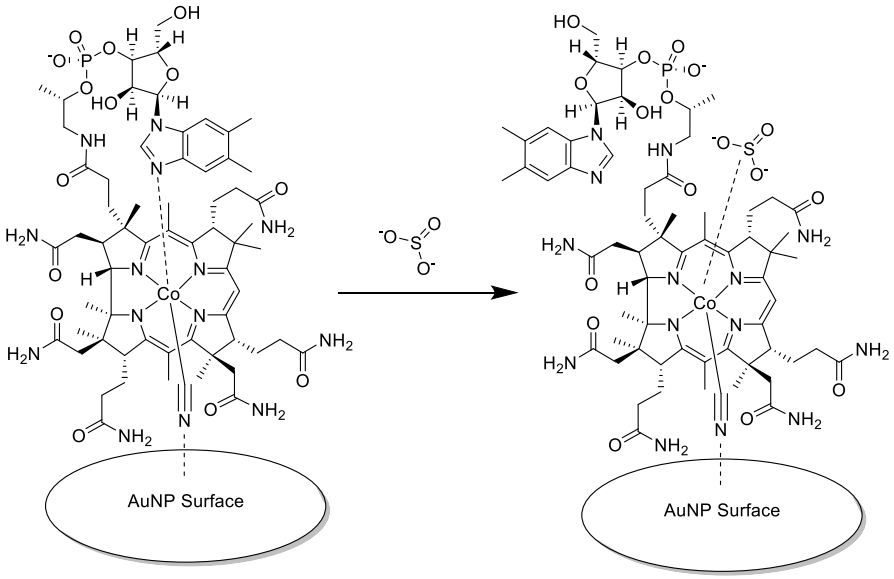
Paul Denman *, Kevin Jack [+], James Blinco[Ψ], Idriss Blakey *

** Australian Institute of Bioengineering & Nanotechnology and Centre for Advanced Imaging, University of Queensland, St Lucia, Queensland 4072, Australia*

[+] Centre for Microscopy and Microanalysis, Australian Institute of Bioengineering & Nanotechnology, University of Queensland, St Lucia, Queensland 4072, Australia

[Ψ] School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology, Brisbane, Queensland 4001, Australia

Surfaced Enhanced Raman Spectroscopy (SERS) is a highly sensitive, powerful technique for detection of small molecules down to single molecule levels. Combined with the rich spectrographic information provided, SERS is a highly attractive technique for the development of chemical sensors. Although many highly sensitive SERS substrates have been developed, direct detection and quantification of analytes in complex solutions still provides a challenge. One way to overcome this is to use a reactive probe in combination with gold nanoparticles which provide a high SERS enhancement upon aggregation to provide sensitive selective detection and quantification of a target analyte.
Here we report on using Vitamin B12 (VB12) as a reactive SERS probe. It is advantageous in this role because it has a highly conjugated corrin ring which provides a large Raman scattering cross section, a cyanide ligand which can act as an anchoring point toward the gold surface and cobalt has the potential to act as a binding point for certain analytes. We demonstrate that gold nanoparticles coated with VB12 can be used to give a ratiometric SERS signal for the quantification of sulphite in complex solutions such as wine down to nano-molar concentrations. The binding of VB12 to the gold may be essential to the sensitivity of the system, because it significantly enhances the reactivity of the VB12 towards the sulphite anion.



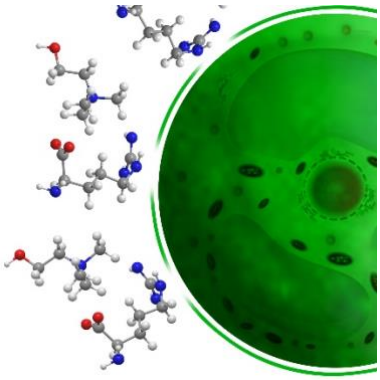
Possible reaction mechanism of Sulphite with VB12

B9 - The ionic liquid cholinium argininate is an efficient solvent for extracting high-value *Nannochloropsis* sp. lipids.

Elvis T. Chua* [1], Manuel Brunner [2], Rob Atkin [2], Eladl Eltanahy [1,3], Skye R. Thomas-Hall [1], and Peer M. Schenk [1]

1 Algae Biotechnology Laboratory, School of Agriculture and Food Sciences, The University of Queensland, Brisbane, QLD 4072, Australia
2 School of Molecular Sciences, The University of Western Australia, Perth, WA 6009, Australia
3 Phycology Laboratory, Botany Department, Faculty of Science, Mansoura University, Mansoura 35516, Egypt
Corresponding author's email address: e.chua@uq.edu.au

Microalgae can be grown for food, feed and fuel without competing for arable land or freshwater resources. However, the extraction of microalgal oil has been challenging thus far. *Nannochloropsis* sp. has been a very attractive microalgal species because of its high omega-3 fatty acid content in its oil. However, it is also one of the species with the strongest cell wall. Currently, energy-intensive mechanical techniques and harmful and flammable organic solvents are used for extracting lipids from *Nannochloropsis* sp. biomass. Thus, in this study, cholinium amino acid [Ch][AA] based ionic liquids (ILs) were investigated for their capability to extract lipids from *Nannochloropsis* sp. Among all the ILs tested, cholinium argininate ([Ch][Arg]) extracted the highest amount leaving only 1.4±0.2% lipid in the remaining biomass. The extraction was still efficient at room temperature leaving only 7.9±0.3 % lipid. Thus, [Ch][Arg] is an efficient "green" solvent for *Nannochloropsis* lipid extraction. Current efforts focus on oil recovery from the IL layer and suggestions from conference participants will be considered.



B10 - HPLC-Based Method Used to Determine Whole Cell Sialic Acid in Biological Samples.

***Porter, Z.*, Schweiker, S., Levonis, S**

Faculty of Health Sciences and Medicine, Bond University, Robina, Australia

zoe.porter@student.bond.edu.au

Sialic acids represent a family of 9-carbon acidic monosaccharides that naturally reside on the surface of most eukaryotic cells and soluble proteins (1). The expression of surface sialic acids is significantly increased in cancer cells, creating a distinct hypersialylated state strongly associated with malignant disease progression and oncogenic transformation (2-4). The developed method has been designed to quantify sialic acids in biological samples (obtained from cell culture) using high performance liquid chromatography with ultraviolet detection (HPLC-UV). The developed HPLC-UV based method uses ion-pairing chromatography to determine the concentration of sialic acid (Neu5Ac) in HeLa and RT-4 cells. Neu5Ac separation was achieved using a C18 reverse-phase column and an isocratic mobile phase with triisopropanolamine as the ion-pairing reagent. Flow rate and wavelength were set to 0.4ml/min and 215nm respectively. Cells were cultured in Dulbecco's Modified Eagle's Medium containing 10% fetal bovine serum over 70 hours. Sialic acids were isolated in their free form using ethanol precipitation and acid hydrolysis. Whole cell Neu5Ac concentration was then assessed via HPLC-UV. Spiking and inter/intra-day experiments were completed. The three spiked samples of Neu5Ac had a percentage recovery of 115.81%, 109.33% and 104.6% respectively, falling within the acceptable recovery range of 80%-120%. The inter/intra-day precision and accuracy results for Neu5Ac concentrations 0.05, 0.1, 0.2, 0.3 and 0.4mM each had a CV <15% and accuracy percentages within the ±15% accepted range. LOD and LOQ values were determined at 0.0055mM and 0.0167mM respectively. The number of theoretical plates was calculated at 5771. The precision, accuracy, and reproducibility of the developed method has been validated as per FDA guidelines, signifying the effective design of a robust analytical method capable of measuring whole cell Neu5Ac.

[1] Varki, A. (2008). *Trends in molecular medicine*, 14(8), 351-360.

[2] Büll, C., Stoel, M. A., den Brok, M. H., & Adema, G. J. (2014). *Cancer research*, 74(12), 3199-3204.

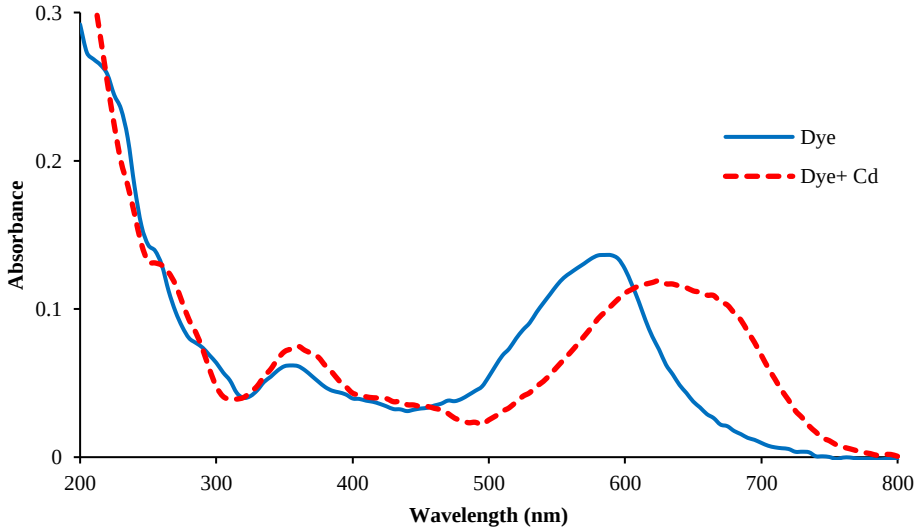
[3] Pearce, O. M., & Läubli, H. (2015). *Glycobiology,* 26(2), 111-128.

[4] Vajaria, B. N., Patel, K. R., Begum, R., & Patel, P. S. (2016). *Pathology & Oncology Research*, 22(3), 443-447.

B11 - Optical sensor for detection of heavy metal pollutants in aqueous medium

Mahnaz D. Gholami*, Emad L. Izake, Godwin A. Ayoko, Prashant Sonar
md.gholami@hdr.qut.edu.au

A new water soluble azo derivative of benzothiazole has been synthesised and characterised by ^{1}H NMR, ^{13}C NMR, FT-IR spectra and Mass spectroscopy. The new benzothiazole dye showed a strong UV absorbance at 585 nm that shifts to 635 nm in the presence of cadmium ions (Cd^{+2}). Therefore the new dye was utilised as an optical probe for the detection of Cd^{+2} contamination in water where its colour changed from pink to green in the presences of the metal ion at pH12. The stoichiometry of the complex formation between the new dye and the cadmium ion was found to be 2:1, Dye: Cd (II). The selectivity of the dye towards other metals was also studied and only Zn and Cu ions caused interference. Finally the new dye was used for the quantitative analysis of Cd^{+2} down to 10^{-6} Molar.



B12 - Physicochemical characteristics of commercial strawberry cultivars grown in Australia

Shammy Sarwar*, Michael E Netzel, Hung Hong Trieu and Yasmina Sultanbawa

Queensland Alliance for Agriculture and Food Innovation (QAAFI), The University of Queensland, PO Box 156, Archerfiled BC, QLD 4108, Australia

**shammy.sarwar@uq.edu.au*

Strawberries are a popular fruit in Australia and many other countries because they are considered as tasty and healthy. Depending on the cultivar and growing environment, strawberry can present a rich dietary source of bioactive phytochemicals such as anthocyanins and vitamins such as vitamin C and folate. Four commercial strawberry cultivars grown in Australia (Red Rhapsody, Ruby gem, Fortuna and Festival) were analysed for their physicochemical characteristics as well as anthocyanin content (main phytochemical in strawberry and responsible for its red colour).Titratable acidity (TA), total soluble solids (TSS), pH, moisture content and colour were determined by standard methods whereas anthocyanins were analysed by UHPLC. There were only slight differences in total soluble solids (8-10.5%), titratable acidity, pH, moisture content (86.7-90%) and colour, whereas a significant difference could be measured in total anthocyanins ranging from 19.3 ± 0.9 mg/100 fresh weight in Ruby gem to 30.5 ± 1.4 mg/100 g fresh weight in Red Rhapsody. The results of this pilot-study indicate that commercial strawberry cultivars have very similar physicochemical characteristics but can differ considerably in their phytochemical composition and subsequently nutritional quality.

B13 - Native Australian Fruits: freeze-dried Kakadu plum (*Terminalia ferdinandiana*) powder as an example for a high-quality food product

Eshetu M Bobasa*[1], Michael E Netzel[1], Stan Kubow[2], Mirudsmita Chaliha[1], Anh Dao[1], Yasmina Sultanbawa[1]

[1] *Queensland Alliance for Agriculture and Food Innovation (QAAFI), The University of Queensland, 39 Kessels Road, Coopers Plains, QLD 4108, Australia*

[2] *School of Human Nutrition, McGill University, 21,111 Lakeshore Road, Ste. Anne de Bellevue, Montreal, QC H9X 3V9, Canada*

e.bobasa@uqconnect.edu.au; e.bobasa@uq.edu.au

Polyphenols and vitamins have become major targets in the functional food and nutraceutical industries due to their abundance in plant food and reported health benefits for humans. *Terminalia ferdinandiana*, commonly known as Kakadu plum, is a native Australian fruit that contains several important secondary metabolites/bioactive compounds such as vitamin C and ellagic acid, a polyphenol.

Since Kakadu plum is a natural produce, its composition and subsequently vitamin C and ellagic acid content can vary considerably depending on the cultivar, collection/harvest season and especially processing. Therefore, the aim of the present study was to assess the vitamin C and ellagic acid content in freeze-dried Kakadu plum powder (a common product in the food industry) by UHPLC. The Kakadu plum fruits were grown and picked in the Northern Territory, Australia.

The freeze-dried Kakadu plum powder (produced according to standard procedures) had an outstanding vitamin C content of 200 mg/g DW (98.5% L-ascorbic acid and 1.5% dehydroascorbic acid) and a total (free and bound) ellagic acid content of 4658 mg/100g DW.

The results of this pilot-study clearly demonstrates that vitamin C and ellagic acid, the main bioactive compounds in Kakadu plum, could be retained at a high level in freeze-dried fruit powder (an important industry product) indicating its nutritional and functional food quality.

B14 - Strawberries – Higher in folate than previously thought!

Michael E Netzel[1*], Nadine Weber[1,2], Caroline Dumler[1,2], Lisa Striegel[2], Anh Dao Thi Phan[1], Hung Hong Trieu[1], Michael Rychlik[1,2], Tim O'Hare[1]

[1]Queensland Alliance for Agriculture and Food Innovation, The University Of Queensland, Coopers Plains, QLD 4108, Australia, [2]Technical University Munich, Freising/Munich, Germany

m.netzel@uq.edu.au

Folate is considered a critical vitamin and folate deficiency is associated with neural tube defects in newborns. Strawberries are considered a tasty fruit by many consumers and may potentially be a more important dietary source of natural folates than previously thought. Recently, more than 30 Australian-grown strawberry varieties and experimental breeding lines were analysed for total folate and individual folate vitamer profiles by Stable-Isotope-Dilution-Assay. The total folate content ranged from 70-164 µg/100 g fresh weight, which was well above the value currently in the FSANZ NUTTAB database (39 µg/100 g fresh weight). With these high folate concentrations, a single serve (1 cup or 144 g) of Australian-grown strawberries would deliver almost 60% of the FSANZ recommended dietary intake (RDI) for folate. Furthermore, folate concentration in the outer strawberry tissue was found to be about 1.5-fold higher than the inner tissue of the fruit. 5-methyltetrahydrofolate, a biologically active form, was the principal vitamer present in both inner and outer tissue. This difference in distribution of folate between outer and inner tissue could indicate that flatter, longer strawberries may have greater potential to accumulate folate than fruit of a more spherical shape.

This study was partly funded by Horticulture Innovation Australia Ltd. project 'Naturally Nutritious' (HN15001).

B15 - The application of ICP-OES spectroscopy to the accurate determination of phosphorus in matrix-dense rock solutions.

Marietjie Mostert
School of Earth and Environmental Sciences, The University of Queensland
m.mostert@uq.edu.au

Phosphorus is a minor constituent of earth materials, especially silicate rocks and iron ores. Its accurate determination is, however, essential, especially in the steel industry, as phosphorus embrittles steel (Thermo Scientific, 2011). Iron ores which contain more than ~ 0.02% phosphorus in not suitable for modern blast furnaces (Abraham J. B. Muwanguzi, 2012). For beneficiation purposes, iron ore vendors therefore need rapid and accurate analysis for phosphorus and other deleterious elements.

Other elements impacting on the quality of steel raw material are fairly straightforward to determine. Phosphorus presents difficulties, as the traditional analytical method (XRF) is subject to many inter-elemental and matrix interferences (Norrish, 1969). An alternative analytical approach is fusion and analysis by ICP-OES. This also present a number of problems which include low sensitivity, matrix interference, and interferences by Fe and Cu on the most sensitive spectral lines for phosphorus. Also, the abundance of phosphorus in these matrices is low, generally under 0.1% weight, therefore requiring the use of the most sensitive spectral lines available.

This paper investigates refinements to the existing technique of measuring phosphorus in rocks by preparation by fusion and analysis by ICP-OES. Spectral analysis, mathematical modelling and specific software applications are compared with each other against existing certified values for phosphorus as determined by inter-laboratory testing generally and by XRF specifically.

Abraham J. B. Muwanguzi, A. V. (2012). Characterization of Chemical Composition andMicrostructure of Natural Iron Ore from Muko Deposits. *ISRN Materials Science, 2012*(Article ID 174803). doi:10.5402/2012/174803

Guider, J. W. (1981, April). Iron Ore Beneficiation - Key to modern steelmaking. *Mining Engineering, 33*, 410-413.

Michael V. Ruby, A. D. (1994). In Situ Formation of Lead Phosphates in Soils as a Method to Immobilize Lead. *Environmental Science and Technology, 26*, 646-654.

Norrish, K. a. (1969). An accurate X-ray spectrographic method for the analysis of a wide range of geological samples. *Geochimica et Cosmochimica Acta, 33*, 431-453.

Thermo Scientific. (2011, June). *Downloads/Penalty-Elements-in-Iron-Ore-App-Summary-low-2011Jun23.pdf*.

B16 - The effect of physiological maturity and different cooking methods on anthocyanin accumulation in purple sweetcorn kernels

Hung T. Hong*, Michael E. Netzel, Tim J. O'Hare

Centre for Nutrition and Food Sciences, Queensland Alliance for Agriculture and Food Innovation (QAAFI), The University of Queensland, PO Box 156, Archerfield BC, QLD 4108, Australia

h.trieu@uq.edu.au

Anthocyanins are natural pigments and a major a subclass of polyphenols/flavonoids found in a wide range of fruits and vegetables. Anthocyanins vary in their structure, differing slightly in hydroxylation and glycosylation patterns of the main ring structure. Recent studies indicate that anthocyanins or their derived products may have beneficial effects on human health.

The aims of the present were to determine the effects of (a) six different stages of maturity and (b) different cooking methods on the accumulation and retention of anthocyanins in purple sweetcorn kernels. Analysis was performed by UHPLC-PDA-MS/MS.

A total of nine main anthocyanin compounds, namely cyanidin-3-glucoside, cyanidin-3-(6''-malonyl)glucoside, cyanidin-3-(3'',6''-dimalonyl)glucoside, peonidin-3-glucoside, peonidin-3-(6''-malonyl) glucoside, peonidin-3-(dimalonyl)glucoside, pelargonidin-3-glucoside, pelargonidin-3-(6''-malonyl)glucoside, pelargonidin-3-(dimalonyl)glucoside and pelargonidin-3-(malonylsuccinyl) glucoside were identified and quantified in uncooked purple sweetcorn samples, ranging in physiological maturity from 20 to 40 days after pollination (DAP).

Total anthocyanin content (TAC) increased with kernel physiological maturity, peaking between 32 and 36 DAP with a TAC between 50.7 and 58.7 mg/100g FW. Interestingly, the increase in TAC appeared to be related to an increased progression of purple pigments across the surface of the maturing kernels. The coverage of purple pigment was initiated as a small spot at the stigma-end of the kernel, gradually spreading over the kernel surface towards it's point of attachment to the cob, so that eventually the kernel pericarp appeared almost completely purple.

Furthermore, four different cooking methods (microwaving, steaming, boiling in bag and pan-frying) were investigated. A significant ($p<0.05$) decrease in TAC of 30% was observed in the kernels after pan-frying and microwaving whereas steaming and boiling appeared less detrimental to anthocyanin decline. Our findings are important in regards to the development of strategies to maximise and maintain anthocyanins in purple sweetcorn, and as a consequence improve its potential nutritional quality.

C8 - Ketol-acid reductoisomerase (KARI) Inhibitors as Potential Anti-Tuberculosis Prodrugs.

Julia L. Kurz*, Tenuun Bayarra, Khushboo M. Patel, Waleed M. Hussein, Nicholas P. West, Gerhard Schenk, Luke W. Guddat, Ross P. McGeary

School of Chemistry and Molecular Bioscience, University of Queensland, Brisbane, Australia

Julia.kurz@uq.net.au

Tuberculosis (TB) is an infectious disease which poses a significant threat to global human health. TB is so problematic due to the development of multi-drug resistant strains. Therefore, there is an urgent need to develop new TB drugs. Ketol-acid reductoisomerase (KARI) is a metallo-enzyme present in bacteria which is involved in the synthesis of branched chain amino acids. This pathway has been shown to be vital for bacterial survival, making it an attractive drug target. Additionally, this pathway is not present in animals, allowing potent inhibitors of KARI to be toxic to bacteria without impacting the human host. This project aims to design and synthesise novel KARI inhibitors based on previous lead compounds, using techniques such as computational docking, and structure activity relationship studies, before testing them against the isolated KARI enzyme. These inhibitors will operate by a novel mechanism of action, bypassing TB's current resistance mechanisms. Another challenge when developing anti-TB agents is the bacteria's lipid-rich cell wall, which can be difficult to penetrate. We aim to utilise the prodrug approach to allow our inhibitors to penetrate the cell wall and reach their target, the KARI enzyme. The ultimate goal is for these compounds to be used as drugs to treat TB in humans.

C9 - Development of computational tools for the rational design of heparin/glycosaminoglycan mimetics

Eric Boittier*[a], Neha S. Gandhi[b], Vito Ferro[a]

[a]School of Chemistry and Molecular Biosciences, The University of Queensland, St Lucia QLD, 4017

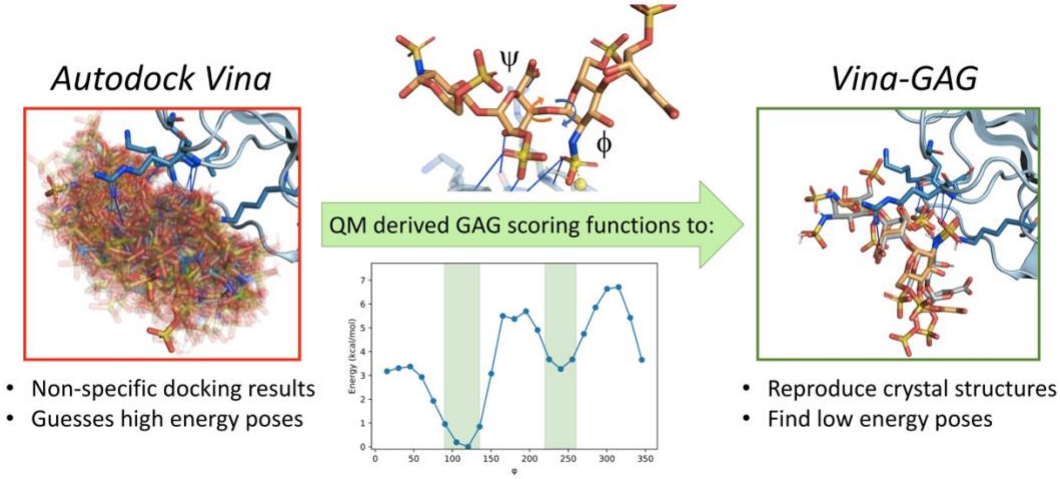
[b]Queensland University of Technology, Science and Engineering Faculty, Gardens Point QLD, 4000

eric.boittier@uqconnect.edu.au

Glycosaminoglycans (GAGs) are a family of highly sulfated polysaccharides found on the surface of all eukaryotic cells. Heparin, a member of the GAG family, is a widely used anticoagulant and possesses the highest negative charge density of all biomolecules. GAGs are involved in various physiological and pathological processes such as neuronal development, cancer and osteoporosis.

Understanding protein-GAG interactions requires a concerted effort between experiment and computational study. However, modelling their high negative charge density and immense conformational space is an ongoing challenge for computational chemists. The glycosidic linkage between sugars has two axes of free rotation: ψ and φ. L-Iduronic acid, an important monosaccharide found in GAGs, and its ability to flip between $^{1}C_{4}$ and $^{2}S_{O}$ ring conformations, adds an extra layer of complexity. It is believed that in some cases, the plasticity of L-iduronic acid allows for selective binding/unbinding to proteins.

Our research involves (1) the development of a bespoke data-mining tool to characterise GAG-protein complexes from the Protein Data Bank, (2) calculations of ψ and φ rotational energy profiles of GAGs using modern quantum mechanics (QM) functionals, and (3) implementation of this work into the premier docking program, Autodock Vina, as a scoring function for identifying novel and biologically relevant GAG-protein interactions. The output of this program will allow for further investigation and validation of these complexes using classical molecular dynamics programs, such as Gromacs and Amber, as a pipeline to rationalise the design of GAG mimetics.



C10 - TD-DFT Investigation of the ESIPT Mechanism of Optoelectronic Materials

Ras Baizureen Roseli[1,3], Ilene Allison[1,3], Ebinazar B. Namdas[2,3], Shih-Chun Lo[1,3], Elizabeth Krenske[1]

[1]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, QLD 4072, Australia

[2]School of Mathematics and Physics, The University of Queensland, Brisbane, QLD 4072, Australia

[3]Centre for Organic Photonics & Electronics, The University of Queensland, Brisbane, QLD 4072, Australia

r.roseli@uq.net.au

Excited-state intramolecular proton transfer (ESIPT) has attracted much attention for the development of highly fluorescent materials. ESIPT is a photoinduced enol-to-keto tautomerisation via proton transfer in the excited state. In the ground state, absorption takes place in the enol (E) form while in the excited state, emission occurs from the excited keto (K*) form, inducing a large Stokes shift which is a desirable property for optoelectronic applications.

ESIPT, like many other excited-state processes, is difficult to predict *a priori*. In this study, linear and non-linear response time-dependent density functional theory (TD-DFT) techniques have been employed to investigate the ESIPT mechanism. TD-DFT has proven to provide useful predictions at a comparatively low computational cost. This work aims to obtain insight into the molecular level processes as a key step in the design of new optoelectronic materials.

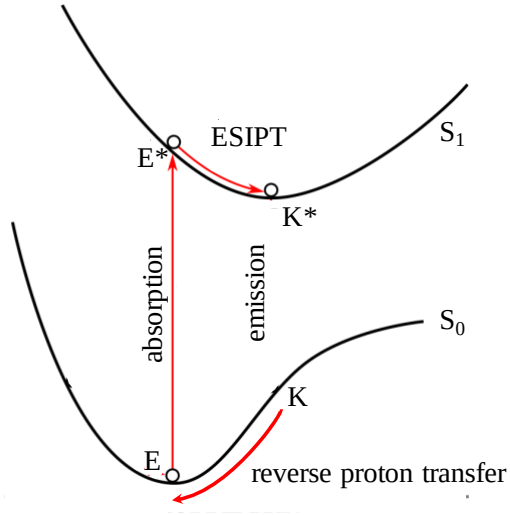


Figure 1: Illustration of a typical ESIPT photocycle

C11 - Recycling Organophosphorus Catalysts for Greener Chemistry: Computational Studies into the Mechanism of Phosphine Oxide Reduction by Organosilanes

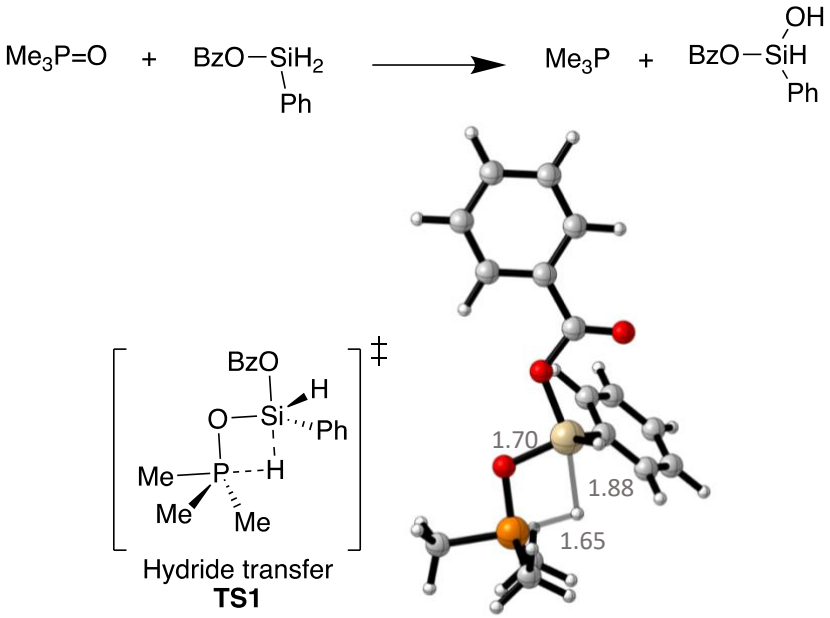
Alicia Kirk*[1], Christopher J. O'Brien[2], and Elizabeth H. Krenske[1]

[1] School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane QLD 4072, Australia

[2] School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland.

alicia.kirk@uqconnect.edu.au

The recycling of organophosphorus reagents, through the organosilane-mediated reduction of phosphine oxides, has been applied to develop catalytic variants of reactions such as the Wittig, Staudinger, and Appel reactions.[1] The ability to recycle phosphine catalysts also enables the use of more expensive phosphines in order to better control stereochemical outcomes in the reactions. A greater understanding of the mechanism of these reactions is required in order to design more active catalysts and improve reduction rates. This includes determining the mechanistic role of acid additives, whose role in accelerating the reduction is unknown.



Density functional theory calculations have been carried out to address this question. The reduction is calculated to occur via a hydride transfer through a four-membered, frontside transition state. Various possibilities were considered to account for the rate enhancing effect of the acid catalyst, including hydrogen bonding between the acid and the phosphine oxide, and the formation of a silyl ester. The silyl ester model appears most promising. The understanding gained from these studies will help design catalysts that are easier to recycle.

1. a) E. E. Coyle, B. J. Doonan, A. J. Holohan, K. A. Walsh, F. Lavigne, E. H. Krenske, C. J. O'Brien, *Angew. Chem. Int. Ed.* **2014**, *53*, 12907-12911; b) C. J. O'Brien, F. Lavigne, E. E. Coyle, A. J. Holohan, B. J. Doonan, *Chem. Eur. J.* **2013**, *19*, 5854-5858; c) C. J. O'Brien, Z. S. Nixon, A. J. Holohan, S. R. Kunkel, J. L. Tellez, B. J. Doonan, E. E. Coyle, F. Lavigne, L. J. Kang, K. C. Przeworski, *Chem. Eur. J.* **2013**, *19*, 15281-15289.

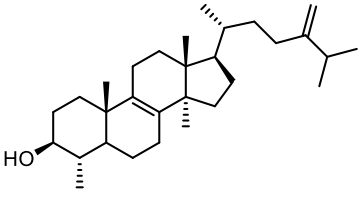
C12 - Synthesis of Intermediates in Steroidal Saponin Biosynthesis

Luke Churchman*, James De Voss

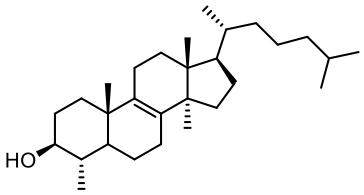
School of Chemistry and Molecular Biosciences, University of Queensland, 4072

Steroidal saponins, a class of structurally diverse terpenoids with a range of bioactivities, are believed to be biosynthesised from cholesterol in several plant species, such as Dioscorea transversa. Cytochrome P450 enzymes are thought to play an integral role in their biogenesis. A subclass of this protein superfamily, CYP51 enzymes are known C-14 steroid demethylases. The sole CYP51 in D. transversa may provide crucial information about the synthesis of the observed cholesterol metabolites in this organism. Chemical synthesis of proposed biosynthetic intermediates are necessary for investigation of this pathway.

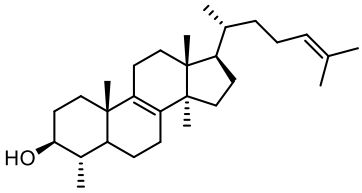
Four potential substrates of the CYP51 from D. transversa were synthesised in this work from commercial lanosterol; 24,25-dihydrolanosterol (94%), 4-demethyl-24,25-dihydrolanosterol (11%), eburicol (6%) and pure lanosterol (20%). An advanced intermediate towards two more potential substrates, obtusifoliol and 4-demethyllanosterol, is also reported. Turnover experiments with CYP51 employing these substrates should provide a greater understanding of the biosynthesis of cholesterol derivatives in D. transversa.



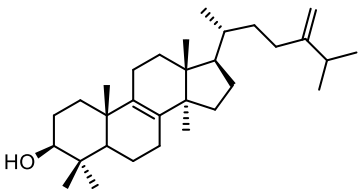
Obtusifoliol
9



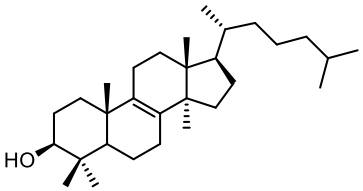
4-Demethyl-24,25-dihydrolanosterol
12



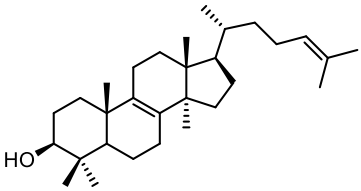
4-Demethyllanosterol
18



Eburicol
19



24,25-Dihydrolanosterol
20



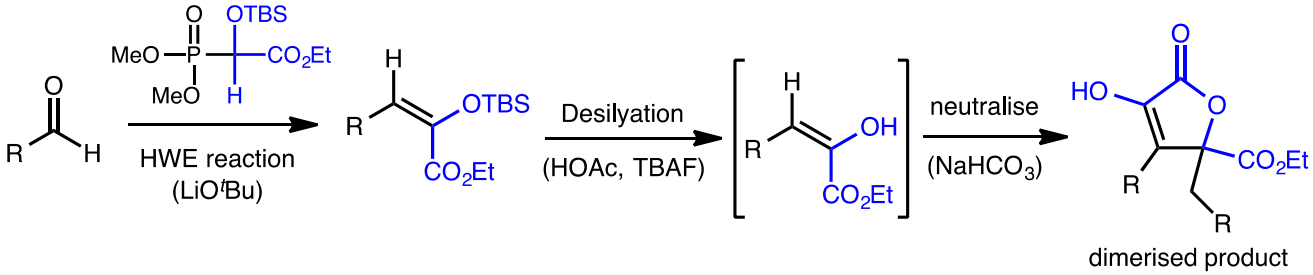
Lanosterol
6

My talk will cover the significance of this work along with the interesting synthetic strategies utilised to produce the desired compounds.

C13 - An unexpected outcome from a Horner-Wadsworth-Emmons reaction

Jack Everson*, Milton J. Kiefel
Institute for Glycomics, Griffith University Gold Coast campus
Jack.everson@griffith.edu.au

A Horner-Wadsworth-Emmons (HWE) reaction is a highly valuable chemical reaction wherein an aldehyde and a stabilized phosphate carbanion react to form the corresponding olefin (usually with E-stereochemistry). As part of our continued interest in the synthesis of higher order sugars,[1,2] we were particularly interested in the reported synthesis of KDO[3] (an 8-carbon sugar that is a key component of Gram-negative bacterial LPS structures) involving the HWE reaction between a simple mannose derivative and a phosphate carbanion. While investigating the scope of this published HWE reaction, we observed a rather unexpected outcome with a range of commercially available aldehydes. After the initial HWE reaction, the silyl enol ether adduct is then treated under standard desilylation conditions, resulting in our case with the formation of a dimerised product (see scheme below). The dimerised product was observed for a range of aromatic aldehydes, and is the dominant product isolated.



This presentation will describe our studies into this unexpected dimerization reaction, including establishing that the dimerised product forms via an aldol-like condensation upon neutralisation of the desilylation reaction. Of particular interest is that the dimerised product contains a butenolide core, and natural products structurally very similar to our dimerised product have shown potent anti-cancer activity.[4]

References

1) Carter & Kiefel, *RSC Advances*, **2018**, *8*, 35768-35775.
2) Williams, Corcilius, Kiefel, Payne, *J. Org. Chem.,* **2016**, *81*, 2607-2611.
3) Feng, *et al*., *Org. Lett*., **2015**, *17*, 2388-2391.
4) Braña *et al*., *Org. Biomol. Chem*., **2004**, *2*, 1864-1871.

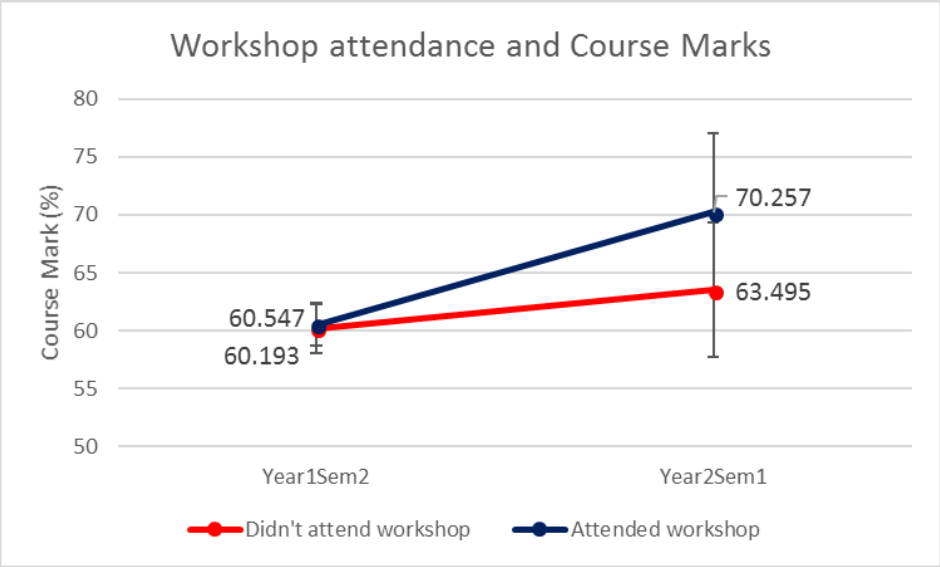
C14 - Breaking Bad – a proactive approach to enhance the transition, engagement and confidence of health students in chemistry

Andrew Pearson*, Jenny Wilson
School of Medical Science, Griffith University, Gold Coast, Queensland, Australia
a.pearson@griffith.edu.au

We identified two groups of students who struggled in their second-year biochemistry course: diploma students entering university at second year, and students who received a grade of 4 in the pre-requisite chemistry course. We designed an early intervention strategy to 1) facilitate the transition of the diploma students to university, 2) revise and consolidate the fundamental chemistry principles, and 3) assist students transition to the content-rich second year biochemistry course.

This intervention strategy was based around the popular television series "Breaking Bad"; the symposium has been held for two days in orientation week each year since 2015. Students have completed workbooks and activities such as the use of molecular model kits and balloons, the chemistry of chocolate, creating 3D models of insulin, cooking curry, and chemistry trivia quizzes.

Participants reported the Breaking Bad symposium eased their transition to university, was very useful to revise their chemistry knowledge, and made them feel positive about learning chemistry: We wanted to determine if attendance at the workshop by at risk students had an effect on their performance in the second-year biochemistry course. A significant main effect for symposium attendance was obtained, $p = .017$, with the mark for the intervention group ($M = 70.26$, $SD = 6.82$) being significantly higher than for the control group ($M = 63.50$, $SD = 5.80$). Our early intervention engagement strategy is an excellent example of a targeted strategy to support a cohort of students to succeed and ultimately successfully complete their university studies as graduates of influence.



C15 - Nano-Chemistry of CalAlSil Porous Polysilicates and Natural Polymers Composites

Dr Leon Burgess-Dean

75 Chataway Street, Carina Heights, Qld, 4152

Email: leon@bricktec.com.au

The use of polymer composites has been extensive over the past three decades but not as much attention has been placed on composites between silicate minerals and natural polymers like cellulose and latex. A novel technique using water-based gelation chemistry has been used to successfully suspend an inorganic-organic composite in an aqueous matrix that cures upon evaporation. The stability of gelation shell and the durability of the cure composite are competing processes that required a detailed examination through multiple test regimes using material combinations consisting of between 12 to 20 unique materials. Inorganic materials were derived from the geopolymer starting materials such as dehydrated clays, oxides and hydroxides of sodium, potassium, calcium, magnesium, aluminium, zinc, iron, nickel, chromium and silica in both crystalline and amorphous forms. Organic polymers include, cellulose, hemicellulose, polysaccharides, cis-1,4-polyisoprene (latex), trans-1,4-polyisoprene, polyacrylic acid, polyacrylonitrile, tetraethyl silicate, decan-2-yl triethylsilicate, triethyloctyl orthosilicate, polydimethylsiloxane, malic acid, acrylic acid, methacrylic acid, oxalic acid and acetic acid. The final material has an amorphous geopolymer chemical motif that is periodically porous at the nano- and microstructural scale. These periodic pores are hybridised with suitable organic polymers and oils to produce a water resistant and sealable composite useable in a variety of applications.

CalAlSil



CalAlSil™ is a revolutionary chemical and materials coating solution. Developed in Brisbane, Australia, CalAlSil™ products:

- Protect against corrosion
- Protect against fire
- Provide ultimate insulation from heat, sound and electricity.

Available as a ceramic, foam, solid or coating, CalAlSil™ offers a cost-effective and portable alternative to existing paints and sealants.

Our product range has multiple industrial applications across the aerospace, building, roads, renewables and 3D printing sectors. For more please visit: www.calalsil.com.au

Leon's Biographical details can be found at the following URL: Leon Burgess-Dean Biographical Details.